A CLINICAL STUDY OF THE EFFECT OF NIFEDIPINE AS PREMEDICANT IN PREGNANCY INDUCED HYPERTENSION

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ANEETA DEVI

C E R T I F I C A T E

This is to certify that the work entitled "A CLINICAL STUDY OF THE EFFECT OF NIFEDIPINE AS PREMEDICANT IN PREGNANCY INDUCED HYPERTENSION" which is being submitted as a thesis for M.D.(Anaesthesiology) Examination 1993, Bundelkhand University, by DR. ANEETA DEVI, has been carried out by the candidate herself in the department of Anaesthesiology, M.L.B. Medical College, Jhansi (U.P.).

She has fulfilled the necessary period of stay in this department as required by regulations of Bundelkhand University.

Dated: 16 MAR 1993

16/3/93

(U. C. Sharma)
M.D., D.A.,
Professor and Head,
Anaesthesiology Department,
M.L.B. Medical College,
Jhansi.

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This thesis fulfils the basic ordinance governing the submission of thesis for M.D. laid down by Bundelkhand University.

Dated: 16.3.93

(D. D. Verma)
M.D., D.A.,
Assistant Professor,
Department of Anaesthesiology,
M.L.B. Medical College,
JHANSI(U.P.)

(GUIDE)

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Dated: 16 3 93.

(Pradeep Sahi)
M.D., D.A.,
Assistant Professor,
Department of Anaesthesiology,
M.L.B. Medical College,
JHANSI(U.P.)

(CO-GUIDE)

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Dated:

Aneeta Devi
(Aneeta Devi)

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C O N T E N T

INTRODUCTION

High blood pressure in association with pregnancy has long been regarded as an ominous sign. Kaplan et al (1962) reviewed chronic renal disease and hypertension associated with pregnancy advised that therapeutic abortion should be carried out if the blood pressure rises to 160/100 mm Hg. Fiarley and Kincaid-Smith (1968) concluded that morbidity and mortality rates mainly related to the fetus, were increased in the presence of hypertension.

Nettles and Flanign (1968) found that documented evidence of high blood pressure before the 20th week of gestation implied the existance of hypertension prior to the pregnancy.

Most significant finding associated with hypertensive pregnancy is the increase in fetal loss. The British perinatal morbidity surgery control week(Butlet and Benham, 1963) recorded both the total number of deliveries in one week taking place after the 28th week of pregnancy and the subsequent fate of the fetus. In all there were 16994 singleton pregnancies and 593 fetal deaths. Mortality figures from three consecutive months were also recorded for comparison.

In all these singleton pregnancies in both primiparous and multiparous women, the overall incidence

of raised maternal blood pressure was 27.5%. The hypertension was graded into three groups according to diastolic blood pressure.

Group I patients (mild hypertension) comprised of 17.4% of pregnancies and suffered only a small rise in blood pressure but nevertheless a diastolic reading above 90 mm Hg.

Group II (moderate hypertension) was associated with a higher rate of perinatal mortality.

Group III (severe hypertension) had highest death rate of all.

Group I patients (10.1%) pregnancies were complicated by a diastolic blood pressure of 100 mm Hg or more and fetal mortality in these patients amounted to an overall perinatal mortality rate of 0.66% representing about one fifth of the total fetal mortality. Fetal mortality rate associated with maternal hypertension was 1.2%.

The reports on confidential enquiries into maternal deaths in England and Wales, first started in 1952 have shown a steady decline in the overall number of maternal deaths. There was an even faster decrease in maternal deaths associated with hypertension during 1962-69 (DHSS, 1972).

The decline in maternal mortality was largely due to improved social conditions and better

antenatal care. In a group of over 70 hypertensive pregnancies the perinatal mortality rate was found to be 20% (Jockes et al, 1976).

The changes in blood pressure that occur during normal pregnancy have been well documented by Mac Gillivray et al (1969). They observed that both systolic and diastolic blood pressure fell to their lowest between the 16th and the 24th weeks. The fall in diastolic blood pressure was greater than that in systolic and both values tended to return to normal at term.

Posture is another important factor in interpreting blood pressure levels in pregnancy. After the 30th week of gestation approximately 10% of all normal pregnant women can develop a profound fall in blood pressure if allowed to remain supine for more than a few minutes.

Wright (1962) showed this to be due to a lowered venous return when the uterus compresses the inferior vena cava while the patient was lying on her back. Kerr et al (1964) using constrast radiography immediately before and after delivery showed inferior vena caval obstruction in 10 of 12 patients studied during late pregnancy. The levels of 139 mm Hg systolic and 89 mm Hg diastolic excluding the time of parturition, have been chosen as the upper limit of normal mainly on

the groups that a rise in perinatal mortality is seen even if higher levels are found only on a single occasion.

Prevention and treatment of pregnancy induced hypertension have learned in the last 10 years. High blood pressure complicates approximately 10% of all pregnancies. Pre-eclampsia, the association of hypertension, proteinuria and oedema, accounts for more than 50% of all the hypertensive disorders of pregnancy and is a major cause of fetal and maternal morbidity and mortality.

Distinguishing between pre-eclampsia and other causes of hypertension on clinical grounds can be difficult because of the lack of specific tests for differential diagnosis. Increased vascular resistance has been claimed as the primary cause of pre-eclampsia, however, a variable hemodynamic profile with relatively high cardiac output, normal filling pressures and in appropriately high systemic vascular resistances is now reported for investigation by most investigators. Imbalance between vasodilator and vasoconstrictor eicosanoids may account for platelet activation and increased responsiveness to pressor peptides. Altered prostacyclin(PGI_2) to thromboxane A_2 (TXA_2) ratio in maternal uteroplacental vascular bed may favour local platelet activation and vasoconstriction contributing to placental insufficiency and fetal distress. Recent

evidence seems to suggest that fetal umbilical placental circulation may be the site of the primary vascular injury.

Hypertension complicates approximately 10% of all pregnancies and accounts for 20% of all maternal deaths. Blood pressure normally decrease in peripheral vascular resistance, reaches its lowest point in the second trimester and then gradually increases to or near pregravid levels at term. Normal pregnant women develop vascular resistance to the pressor effect of angiotensin II, which is precociously lost in women who develop gestational hypertension.

Prostaglandins are involved in the development of this vascular refractoriness. An acute and reversible lesion defined "Glomerular endotheliosis" as the basic pathologic pattern of pre-eclamptic neuropathy although gestational hypertension can be super-imposed on undiagnosed essential hypertension or any of a variety of renal diseases.

Treatment of pregnancy induced hypertension is important because it can adversely influence the health and life of both mother and baby. Therapy is beneficial in terms of immediate pregnancy outcome and is not harmful to the child prevention rather than cure should be the aim in managing hypertensive diseases during pregnancy.

The primary goal when treating gestational hypertension is successful termination of the pregnancy with the least trauma to mother and fetus.

Hypertension in pregnancy treated as :-

1. No restriction, bed rest.
2. Elucidation of some of the mechanisms responsible for blood pressure elevation in pregnancy has permitted therapy to be based on more rational principles. The decreased arterial reactivity encountered in normotensive pregnancy is mediated by prostaglandins, preventive therapy using low dose aspirin is an option to prevent development of proteinuria in pre-existing hypertension and provide prophylaxis, against pregnancy induced hypertension.
3. Antihypertensive therapy using sympathetic inhibition with either methyldopa or alpha and beta adrenoceptor blockade.

Vasodilation with hydralazine, calcium entry blockers (Nifedipine) I/V labetalol or diazoxide is primarily used in severe hypertensive patients.

The use of orally administered Nifedipine in severely hypertensive women is associated with encouraging results.

4. When blood pressure levels greater than 170/110 mm Hg needs antihypertensive therapy for maternal safety.

it remains to be proven to what extent foetal growth and welfare can be improved in women with diastolic pressure levels 85-110 mm Hg when adrenoceptor blocking agents are used for blood pressure control. Therapy improved -

- foetal growth.
- prevention of proteinuria.
- Prevention of respiratory distress syndrome.

5. During long term antihypertensive therapy treatment with pindolol yielded better foetal growth than therapy with atenolol.

The disease and its therapy induced special problems with regard to anaesthetic management and care of the newborn infant. In the anaesthetic management of the pre-eclamptic patients drugs that are excreted un changed by the kidney or that may accentuate liver dysfunction should be avoided. Marked fluctuation in blood pressure should be prevented. Correction of circulating blood volume, anemia and electrolyte disorders should be stored prior to the onset of anaesthesia. If magnesium has been used in large doses and oliguria occurs magnesium toxicity may develop has been used in large doses and oliguria occurs. Magnesium toxicity may develop since the magnesium ions is largely excreted through the kidney. Magnesium toxicity presents as loss of all reflexes coupled with a progressive fall

in blood pressure and respiratory depression and is reversed by I/V administration of a calcium salts.

In general anaesthesia patient should also be infused with a balanced electrolyte solution. Following pre-oxygenation, a sleep dose of an I/V induction a drug is followed by endotracheal intubation and maintenance with enhalation agents.

Hypertension in pregnancy causes high fetal mortality rate. The increased attention now given to the presence of hypertension in pregnancy has reduced the risk of serious maternal complications to a very low level. To obtain the best results in terms of the mother and especially of the fetus frequent and careful assessment of both is required during the antenatal period. Where this has been possible a reduction in fetal mortality has been obtained.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Active management of severe hypertension associated with pregnancy induced hypertension(SPIH) and eclampsia is important in order to minimise maternal mortality and morbidity. Only recently need of treating severe hypertension in eclampsia/SPIH, formerly largely neglected area, is appreciated. It assumes greater significance in countries where eclampsia and SPIH are common. Mode of administration and rapidity of its action form the basis for the selection of adjuvant antihypertensive during such hypertensive emergencies. Parenteral reserpine is routinely used for this purpose in most hospitals in India. However, the use of reserpine has become somewhat obsolete due to its erratic efficacy and side effects. Parenteral diazoxide and nitroprusside had never been popular for use in pregnancy. Parenteral hydrallazine (Apresoline) widely used in West is still not approved for marketing in India.

Pre-eclampsia is classified as :

Mild Pre-eclampsia

When blood pressure is upto 160/100 mm Hg with or without presence of oedema and albuminuria.

Severe Pre-eclampsia

When blood pressure is upto 160/100 mm Hg with oedema and albuminuria, which is more than 3 gms in 24 hours.

Eclampsia

Varying degree of hypertension oedema and proteinuria with convulsions.

Pre-eclampsia is classified as severe if any of the following signs or symptoms develops :

a. Systolic pressure more than 160 torr or diastolic pressure more than 110 torr with the patient at rest.
b. Proteinuria exceeding 5 gm/24 hours.
c. Oliguria of less than 400 ml/24 hours.
d. Pulmonary edema.
e. Headache, visual disturbances or epigastric pain.

The disease has reached the phase of eclampsia when convulsions with loss of consciousness are superimposed. Eclamptic coma denotes the transition from pre-eclampsia to coma without convulsion.

Pre-eclampsia is primarily a disease of the primigravida, in particular the young or old primigravida. When it occurs in a multigravida, there are usually other complications such as diabetes, hypertension, pyelonephritis or multiple pregnancy. The sequelae of these pathologic processes affect the mother, the placenta, and the infant.

Clinical manifestations - in mother include a progressive shift of extracellular fluid from the vascular to the extravascular compartment, resulting in hypovolemia, hypoproteinuria, hyponatremia and a rising hematocrit (indicating hemoconcentration). Cardiac output is often

occurs primarily as a result of gradual placental nutritional failure, while the postpartum loss is predominantly due to prematurity.

Kyuzo Aobi et al (1977) studied the effect of nifedipine and propanolol in pregnancy induced hypertension and control group.

Nifedipine creates little or no effect on the blood pressure in normal subjects (Stone et al, 1980).

AETIOLOGY OF PREGNANCY RELATED HYPERTENSION

No clear explanation of increased blood pressure in pregnancy has been established. Three postulater account for pregnancy related hypertension as follows :

1. Altered homeostatic control with increased plasma volume, total exchangeable sodium, extracellular volume and cardiac output may be accepted as a probable explanation of mild hypertension without pre-eclampsia.
2. An alteration in blood coagulation factors resulting in widespread fibrin deposition in capillaries, in both the placenta and uterus and the maternal kidney, and lungs may account for pre-eclampsia associated with severe maternal hypertension and morbidity or mortality of the foetus.
3. Changes in the humoral factors associated with hypertension.

greater than that of normal pregnancy, while blood flow to liver, kidneys and uterus is always less. Cardiac work is increased by augmentations in systemic resistance, blood viscosity and cardiac output. In severe cases cerebrospinal fluid pressure is greatly elevated and the usual hyperaemia of the respiratory tract is exaggerated producing mucosal edema and increased secretions. The haematologic findings include thrombocytopenia, increased platelet adhesiveness, less factor V, high fibrinogen levels, low plasminogen levels, high levels of plasminogen and fibrinolytic inhibitors increased fibrin degradation products and prolonged thrombin and prothrombin times. The disease is a leading cause of maternal mortality. Factors contributing to death are (a) primary cerebral haemorrhage, (b) sequelae of convulsions (cardiac arrest from hypoxia or pneumonitis from aspiration of gastric contents) (c) eclamptic collapse and (d) associated conditions such as abruptio placenta, renal failure and pituitary necrosis.

The placenta tends to age prematurely and develops infarcts, necrosis and degeneration with fibrin replacement. These changes, together with the decreased uterine blood flow, cause impairment of placental function which is intensified during labour by a marked increase in uterine contractility.

The fetus is at high risk and perinatal mortality is considerably increased. The prepartum loss

HOMEOSTATIC DISTURBANCES

In normal pregnancy a progressive increase in the plasma volume has been well documented and tends to be directly related to fetal weight (Hytten and Painkin, 1963). There is also a gradual rise in total exchangeable sodium in excess of 500 m mol towards the end of pregnancy. Despite the retention of sodium a mild hyponatraemia usually occurs due to a proportionately greater increase in extracellular fluid rather than to entry of sodium into the intracellular space. Although the total exchangeable sodium rises the pregnant patient is much less able to withstand depletion of sodium. If it is withheld or if diuretics are used excessively the mother has a greater tendency to develop hyponatraemia. These changes of increased plasma volume, total extracellular fluid and exchangeable sodium are associated with a gradual increase in cardiac output from about the sixth week of pregnancy. At one time it was believed that cardiac output fill in the last few weeks of pregnancy but it is now thought that this was due to observations on patients in the supine position (Vorys et al, 1961).

These homeostatic changes are very similar to the results of deoxycorticosterone are very similar to the results of deoxycorticosterone acetate administration which is, however, associated with hypertension whereas the homeostatic and cardiodynamic changes in normal pregnancy are not. Moreover, the plasma volume increase

is less striking or absent in pregnancy with more severe hypertension.

Schewitz (1971) observed hypertensive pregnant patients and showed contradictory results with sodium and water homeostasis. The use of diuretics may well have distorted some of the results where no increase or even depletion of sodium and water was reported. The accepted view at present is that hypertensive mothers have smaller increase in plasma volume, total exchangeable sodium, and extracellular fluid than normal pregnant women(Chesley, 1972). These observations make it difficult to believe that sodium and water retention can be an important primary factor in the causation of pregnancy related hypertension.

COAGULATION FACTORS

In pre-eclampsia the widespread fibrin deposition particularly related to the capillaries in the maternal kidney and lungs as well as in the placenta, is unlike that found in malignant hypertension which is predominantly in the arterioles. It is also striking that retinal haemorrhages, retinal exudates and involvement of the retinal arteries are rare in pre-eclampsia. Evidence that eclampsia fibrin capillary depositions are primary as opposed to secondary phenomena is lacking. It is well established that in normal pregnancy there is an enhanced ability to produce fibrin and a reduction in fibrinolytic activity during the second and third trimester(Woodfield

et al, 1968). The formation of fibrin rises sharply at the commencement of labour (Bonnas et al, 1969) acting as a protective mechanism for the highly vascularized raw uterine surface after separation of the placenta. The possibility must exist that in pre-eclampsia the sudden increase in fibrin production is set in motion before labour commences, resulting in widespread deposition in maternal organs as well as possibly in the placental circulation where it gives rise to acute fetal distress.

HUMORAL FACTORS

(a) Renin

The possibility that humoral or hormonal factors are predominantly responsible for hypertension in pregnancy has to be considered seriously. Many observations have shown that plasma renin activity is raised in normal pregnancy, as it is also in women taking the contraceptive pill, but that it is lower and may be normal in patients with pre-eclampsia. There is little evidence of absolute levels of angiotensin II in pregnancy, but pregnant women are less sensitive as regards raised blood pressure response to infusions of angiotensin(Chesley et al,1963).

(b) Aldosterone

Renin is known to stimulate aldosterone secretion and as would be expected higher levels of plasma aldosterone are found in normal pregnancy. As with plasma renin

activity, aldosterone levels are decreased in mothers with high blood pressure (Rinsler and Rigby, 1957). It is again difficult to accept that aldosterone can play an important part in the significant hypertension associated with increased foetal mortality.

(c) Oestrogen and Progesterone

There is no evidence that production of either oestrogen or progesterone can account for severe hypertension in pregnancy. Although hypertension is occasionally associated with contraceptive pills containing oestrogen, it is usually only of the milder type. There is a striking low incidence of hypertension in patients receiving high dose oestrogen therapy because of either carcinoma of the prostate or in post menopausal women, carcinoma of the breast. These findings make it unlikely that the high oestrogen production seen with multiple pregnancy or hydatidiform mole is mainly responsible for the increased incidence of pregnancy related hypertension. Further more progesterone may tend to increase renal excretion of sodium either by an antialdosterone effect (Landau and Lugibihl, 1958) or more directly.

DIAGNOSIS OF PREGNANCY RELATED HYPERTENSION

Women who before pregnancy were well documented and non hypertensive may during pregnancy develop hypertension which can be pregnancy related or can arise from a

situation de nova: in the latter case a renal lesion is the likeliest cause and glomerulonephritis is the expected finding. In those patients with known pre-existing hypertension that has not been fully investigated it is very difficult to establish the presence of a unilateral renal lesion or drainage tract abnormality without the use of radiology or isotopic methods. Investigation has to be deferred.

In both the second and third trimester the presence of proteinuria (upto 2 gm/24 hour) is suggested of pregnancy related hypertension. Accurate quantitation of urinary protein excretion cannot be obtained using Esbact's method. A turkimetric procedure using trichloracetic acid or a direct nitrogen estimating method must be used greater levels of proteinuria or selective proteinuria (Rowe and Soothill, 1961) are more suggestive of primary renal disease.

Wagner Kolb and Fischer (1971) investigated patients post partum who had previously been diagnosed as having pre-eclampsia and found chronic renal disease in 30% women. In the early stages or in mild cases of pre-eclampsia, renal biopsies may only show very minor changes and it can be very difficult to differentiate between pregnancy related cardiovascular renal changes and glomerulonephritis arising de nova. In this situation the renal biopsy serves predominantly to exclude the presence of primary renal disease. The striking glomerular

changes showing fibrin deposition in the capillaries and cytoplasmic swelling of the endothelium and epithelium are diagnostic endocrine disease.

Endocrine disorders (diabetes mellitus is the commonest example) are associated with a higher incidence of maternal hypertension compared with normal pregnancy. However, apart from diabetes the overall number of patients presenting with hypertensive disease in pregnancy as a result of endocrine disorders is small.

Pheochromocytoma may give to acute and severe high blood pressure in the first trimester and its presence associated with a maternal mortality rate of over 40%.

Hypertension in the first half of pregnancy is associated with a hydatidiform mole.

Although the hypertension is usually mild and less significant than the other features of this condition sometimes it may be fulminating. Once the mole has been removed the blood pressure reverts to normal vascular anomalies.

Vascular abnormalities such as coarctation of the aorta or stenosis of the renal artery due to muscular hyperplasia may cause hypertension in women of child bearing age, they do not appear to be disclosed by pregnancy.

CLASSIFICATION OF HYPERTENSION

Beilin et al (1974) suggested that blood pressure should be defined in quantitative terms by relating

pressure changes to gestation, the presence or absence of proteinuria and other features such as impairment of renal function as well as to the postpartum blood pressure.

FETAL RISKS

There remains an increased prevalence of premature placental separation in the hypertensive pregnancy, even where good control of blood pressure is obtained. This complication is twice as frequent in moderate hypertension and four times more common in severe hypertension than in non-hypertensive pregnancy. There is an increased rate of placental degeneration and infarction and of necrosis and thrombosis of the placental vasculature. As a consequence, the fetal growth rate is frequently retarded. If these changes occur acutely intrauterine anoxia and intrauterine death may quickly supervene. Intrauterine death, a shorter period of gestation and a greater prevalence of fetal lung immaturity associated with a higher incidence of necessary obstetric intervention are probably the main reasons for the high fetal loss associated with hypertensive pregnancy.

MATERNAL CLINICAL FEATURES

Hypertension in pregnancy may asymptomatic, it is frequently associated with oedema as well as proteinuria. Fluid retention is a common accompaniment of pregnancy, even in uncomplicated pregnancies it has been reported as some stage in as many as 80% (Robertson,1971)

and there is a still higher incidence in the presence of maternal hypertension.

Nylvjesy et al (1968) showed the average weight gain to be higher with mild pre-eclampsia than in non hypertensive pregnancies. In a group of severely pre-eclamptic mothers, Fish et al (1959) showed that the total gain in weight and the rate of gain were not significantly different from those of non hypertensive mothers. Most clinicians agree that dependent oedema is less significant in pregnancy than was previously thought. However, non dependent oedema of the hands and face found in association with maternal hypertension may be the first indication of serious complications.

Hypertensive mothers may also present with general malaise, lassitude, headache, increasing nocturia, diminishing exercise tolerance and a higher than normal incidence of uterine bleeding or antepartum haemorrhage. Eclamptic fit may occur and can prove fatal. Occassionally mothers with mild hypertension may experience eclamptic fits.

The principal cause of death in eclampsia by clinical finding were pulmonary oedema (46.6%), acute myocardial failure and cerebral haemorrhage (11.6% each), anemia (7.8%), hyperpyrexia (5.8%), post partum haemorrhage (4.8%), and asphyxia, obstetric shock and accidental haemorrhage (3.9% each). Lahiri (1970), Goswami and Goswami (1984) and Sarbar (1986) also

reported the principal causes to be cardiac failure, pulmonary oedema, cerebral haemorrhage and shock.

Brown (1950) stated that when blood pressure rises above 160/100 mm Hg the spasm of glomerules arterioles causes albuminuria. Present study also confirms the significantly higher incidence of proteinuria. Das (1968) and the Obald (1968) have also reported a similar finding.

The medical treatment of pre-eclampsia consists of three fundamental facets:

a. Rest, (b) diet including regulation of fluid and electrolyte balance and (c) drugs i.e. sedatives antihypertensives and magnesium sulfate. Plasma expands therapy with human albumin was recently shown to be most beneficial. Circulating blood volume increased, placental blood flow, improved, depleted protein was replaced and urine output increased while diastolic pressure and edema declined. Of the antihypertensive drugs, veratrum alkaloids and reserpin cause bradycardia, apresoline tachycardia, Magnesium sulfate is a depressant of the peripheral neuromuscular junction. Magnesium is helpful in producing vasodilatation and decreasing uterine contractility, thus lowering vascular resistance and blood pressure and increasing uterine blood flow. Diuretics agents are rarely indicated in pre-eclampsia.

For the treatment of severe pre-eclampsia, continuous extradural block to a level of the eighth thoracic segment to denervate uterus, kidney and adrenals has proven to be a valuable adjunct in patients, whose blood pressure does not decrease with conventional methods or whose blood pressure rises again markedly during labor. Similarly regional blockade has been used with advantage in the therapy of eclamptic coma awakening appears to occur readily, urine production increases and the blood pressure is controlled easily.

Eclamptic convulsions are treated according to the same principles as convulsions from other causes i.e. by the combination of (a) oxygenation, (b) control of muscular hyperactivity (succinylcholine), (c) depression of cortical electrical seizure activity (ultrashort acting barbiturate or diazepam), (d) therapy for metabolic acidosis (sodium bicarbonate).

ANAESTHETIC MANAGEMENT

The disease and its therapy induce special problem with regards to anaesthetic management and care of the newborn infant. Anemia is marked by the rising hematocrit compensation to the effects of sympathetic blockade during regional analgesia is decreased by hypo volemia, hyponatremia and the action of the antihypertensives and magnesium sulfate. If magnesium has been used in large doses and oliguria occurs, magnesium

toxicity may develop since the magnesium ion is largely excreted through the kidney. Magnesium toxicity presents as loss of all reflexes coupled with a progressive fall in blood pressure and refractory depression and is reversed by intravenous administration of a calcium salt (calcium gluconate or chloride). Magnesium by virtue of its neuromuscular blocking properties, potentiates the effect of all muscle relaxants. Infants of mothers treated with large doses of magnesium sulfate may develop clinically significant hypermagnesemia with hypocalcemia that does not respond to calcium therapy but necessitates assisted ventilation and lavage until the muscle weakness has subsided. Neonates whose mothers received reserpine may have respiratory obstruction from nasal congestion, this can be treated simply and effectively by installation of neosynephrene nasal drops.

In the anaesthetic management of the pre-eclamptic patient, drugs that are excreted unchanged by the kidney or that may accentuate liver dysfunction should be avoided marked fluctuations in blood pressure should be prevented. Correction of circulating blood volume and electrolyte disorders should be started prior to the onset of anaesthesia. For labor and vaginal delivery regional analgesia produces optional conditions. The degree of maternal circulatory and cerebrospinal fluid pressure responses to the pain of contractions is reduced and the hazards of a

hypertensive crises is minimized. The incidence and severity of neonatal depression appears to be significantly lower following regional as compared with general anaesthesia. For labour with slow progress a double catheter extradural block is best for labour with rapid progress. A spinal or single injection extradural block is suitable. Epinephrine should not be added to the anaesthetic solution because eclamptic patients are particularly sensitive to its chronotrophic effect. Paracervical block is not recommended because this technique is associated with a considerable incidence of foetal depression when used in the presence of placental insufficiency. When regional analgesia cannot be employed, pudendal block may be combined with inhalational analgesia (40% N_2O or 4% cyclopropane or 2% fluroxene in O_2). Diethyl ether, methoxyflurane and halothane are not the agent of choice.

For caesarean section, the selection of anaesthesia lies between regional analgesia and balanced regional anaesthesia. Regional analgesia, should be used only if central venous pressure measurements indicate that the degree of hypovolemia is not marked. Although extradural analgesia without epinephrine in the anaesthetic solution appears to cause less cardiovascular response in the mother than spinal block, the latter requires only a small dose of drug, which neither takes the maternal

degradative processes nor cross the placenta. Adequate left uterine displacement and acute hydration with balanced electrolyte solution must be used to prevent hypotension. If the blood pressure declines despite these prophylactic measures, a small dose of ephedrine should be injected intravenously. When general anaesthesia is selected, the patient should also be infused with a balanced electrolyte solution. Following pre-exygenation, a sleep dose of an intravenous induction drug is followed by endotracheal intubation and maintenance with inhalation agents, permitting an inhaled oxygen fraction of 50-60%. It should be remembered that if the patient has been receiving magnesium sulfate therapy, succinylcholine will be potentiated to a lesser degree than curare.

Origin of the term caesarean section is obscure. Although generally believed, but it is unlikely, that the term is derived from "Julius Caesar" (Borin, 100 BC) or the Roman Law Lex regia (Eighth century). Existence of such operation is not even mentioned by Hippocrates Galen, Celsus or any other medical writer of that time (Williams Obstetrics).

Caesarean section on dead was practised soon after christian Church gained dominance, as a measure directed at Baptism of the child. The first authorative report about the early use of this operation was published in 1668 by the great French obstetrician Francois Mauricean. The report shows that the operation was

performed on the living in rare and desperate cases and was usually fatal. The situation was same till the end of 19th century because the suturing of uterine wall was not known at that time.

The turning point in evolution of caesarea section came in 1882 when Max Sanger introduced, suturing of uterine wall. First use of extraperitoneal approach by Frank (1907) and lower segment approach by Back(1919) is history by itself. Ken (1926) introduced transverse incision which is the most commonly employed incision to day (Williams Obstetrics).

First use of anaesthesia for caesarean section was done a century ago. During the second half of the nineth century, chloroform and ether were used almost exclusively. Maternal deaths due to aspiration of gastric contents and cardiovascular collapse occurred occasionally. Moreover, because the anaesthesia was often administered in high concentration for intraabdominal surgery, it undoubtedly produced severe depression of the neonates.

Spinal analgesia for caesarean section was first used in 1900 by Doleris and Malartric and lumbar, extradural analgesia was described by Pickles and Jones (1928). Despite their theoretical advantage over general anaesthesia practised at that time regional blocks were infrequently used till fourth decade. However, with improved technique later, the regional blocks became more

and more popular. During period between 1935 and 1942. Out of 562 consecutive caesarean sections 345 were given spinal analgesia. In Israel Zion hospital (Frederrick Weinhaub, 1942) without a single mortality attributable to anaesthetic.

Hellen et al (1944) gave an account of 1415 deliveries including caesarean in which thiopentone Na upto 2 gms was used. Foetal mortality where foetus was known to be alive before commencement of anaesthesia was 2.4%. They also measured maternal and foetal blood levels of thiopentone in some cases and concluded that there was a delay of about 12 minutes before foetal thiopentone level became equal to maternal level and they claimed that if the delivery was delayed beyond this time foetal blood concentration of thiopentone might reach dangerously high level.

There was no standard method for assessment of newborn upto 1952 and terms like asphyxiated baby and apnoeic baby were frequently used to express the condition of neonates. Virgenia Apgar (1953) described a method of evaluation of the newborn, infant in 1952 which is the standard method of assessment of clinical condition of the neonates even to day. She described five objective signs which pertained to the condition of the newborn and a rating of zero. One or two was given to each sign depending upon whether it was absent or present.

The signs used are heart rate, respiratory effect, reflex irritability, muscle tone and colour. A score of ten indicates a newborn is in best possible condition. The apgar score method was further analysed and developed by Apgar and James (1962) and Crawford et al (1973). It was observed that the colour is the most unsatisfactory sign. All infants are more or less cyanotic at birth because of their high capacity for carrying oxygen and relatively low O_2 content and saturation chart of Apgar score.

The technique of balanced anaesthesia using a sequence of O_2 thiopentone, sucamethonium followed by endotracheal intubation with a cuffed tube and nitrous oxide oxygen (6:4), was described by Hodges and Turnstall (1961). No other drug was used before delivery of the infant except intermittent injections of sucamethonium of required. They claimed that this technique produced minimal foetal depression and is superior to conduction blocks Virgenia B Hartridge and Robert Wilson (1963) proposed a similar technique for balanced anaesthesia. In their technique muscle relaxation was obtained by an intravenous drip of 0.2 percent suxamethonium. This remains the most popular technique of general anaesthesia. Pregnancy induced hypertension for caesarean section even to day. Montgomer (1961) compared this technique with the sequence of tiopentone, suxamethonium, Nitrous oxide -

oxygen and Halothane. He found that the latter causes more foetal depression.

Hyperventilation has been used as an aid to production of unconsciousness but the respiratory alkalosis thus produced in mother may however, causes lowering of foetal PO_2, a delay in the onset of normal respiration and a low apgar score at 1 minute (Holmes Frank, 1963). But Coleman (1967) and Scott et al (1969) did not observe any harmful effect on the neonates due to hyperventilation in mother.

To improve foetal oxygenation during caesarean section Rorke et al (1968) studied the effect on neonate of giving 33, 66 and 100 percent oxygen during anaesthesia to the mother. They observed that the foetal oxygenation can be improved by increasing maternal PaO_2, but to a maximum level of about 300 Torr, which can be achieved if inspired gas mixture has about 66 percent oxygen. Above this level of maternal PaO_2 foetal oxygenation deteriorates probably due to vasoconstriction in placental vasculature in response to high PaO_2. They observed high Apgar score in infants born to mother who were given 66 percent oxygen. Anis Bacaba (1970) advocated maternal hyperventilation with 50% oxygen in inspired gas mixture for optimal foetal oxygenation. But when a high oxygen concentration with less nitrous oxide is used then some supplementary anaesthesia is often required to ensure consciousness of the mother. Moir (1970) used halothane for this purpose.

He compared nitrous oxide oxygen in ratio of 70:30 unsupplemented and 50:50 with 0.5 percent halothane. High incidence of low Apgar score (1 to 3) was noticed in the first group and there was no suggestion. that 0.5 percent halothane causes neonatal depression. In fact it improves the condition of the neonate by allowing a higher concentration of oxygen to be administered.

Anis Banaka (1971) compared the incidence of neonatal depression when either propanidio or thiopentone was used for induction of general anaesthesia for elective caesarean section. They reported that the incidence of neonatal depression was higher in the thiopentone group than in the propanidio group, particularly when the induction delivery time was prolonged more than 10 minutes. This was attributed to the different fates of these drugs. Earlier Bradford et al (1969) had got similar results. Other intravenous anaesthetic drugs were studied for using as induction in caesarean section like betamine by Meer et al (1973) and Althesen and drawning et al (1974). Although they did not have any depressing effect on the newborn but they did not offer much advantage over the most commonly used induction agent. Thiopentone while studying the effect of time and lateral tilt Crawford et al (1972) observed greater degree of neonatal asphyxia in non-tilted patients than those who were even given left lateral tilt on operation table.

Kivalo and Saarikoshi (1976) studied the placental transfer of curare and advocated that since curare is able to cross placenta in small but detectable amounts, it is better for the foetal well being to exclude the drug before the delivery especially when the foetal compromise is suspected.

There has been recently an increasing interest in exploring the subtle neonatal effect of drugs used for maternal sedation or analgesia. Scanlon et al(1974) suggested that neurobehavioural testing may present a valuable way to assess the effects of the maternally administered drugs on the newborn infant. This can assess the effect of a more subtle nature than can be measured by Apgar scoring alone. They also devised a neurobehavioural examination which has proved to be simple rapid and reproductable technique of assessing some aspects of the newborn behaviour in the early hours of life.

Several studies have compared the condition of infants delivered by elective LSCS under general anaesthesia with that of regional analgesia was provided (Dalta and Brown, 1977). James et al (1977), Palahniuk et al (1947), Hollman et al(1978), Browning, Houlton and Barclay (1979), Fox et al (1979), the opinion of the majority was that infants delivered under regional anaesthesia were comparatively better condition giving consideration to U.D. interval but not considering the presentation of the infant at the tonic of caesarean

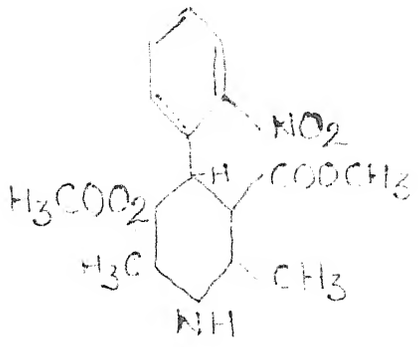
section U.D. interval was relatively prolonged in extradural block. When the U.D. interval was less than 90s the infant born under extradural analgesia was more acidotic than those born under general anaesthesia.

Nifedipine is a calcium channel blocker. Its clinical use since 1973, had been found to be effective and safe in patient having moderate to severe essential hypertension (Morphy et al, 1983). However, it has precise role in hypertension in pregnancy based on control studies has not been established.

The chemical structure of nifedipine |4-(2-nitrophenyl 12-6 dimethyl 3, 5 dicarbomethoxy 1, 4 dihydroxypyridine|.

Nifedipine acts by blocking calcium entry to the smooth muscle thus interfere with excitation and contraction coupling. Given orally it was rapid onset of action and low incidence of serious side effects. Its chief adverse effects are headache, palpitation, cutaneous flushing. No adverse effects in foetus has been documented in clinical use.

Nifedipine has found a place in the management of severe hypertension (Petersons Mikkelsen, 1978) as well as in treating coronary artery spasm (Antman et al,1980).



Nifedipine has been used in pregnancy for inhibition uterine contractions in preterm labour and prostaglandins induced termination of pregnancy where there was uterine hypotonus (Anderson et al, 1979). Its onset of action was not longer than 20 minutes. Hypotensive effect lasted at least 4 hours after 10 mg of nifedipine by mouth. No significant potentiation of the action of nifedipine with administration of other hypotensive agent was seen.

Walters and Redman (1984) successfully used oral nifedipine in 21 patients for acute severe hypertension in pregnancy.

Various antihypertensive agents have been used in pregnancy induced hypertension of methyldopa, hydralazine, diazoxide, beta blockers and diuretics etc.

Nifedipine when combined with propranolol is highly effective because observed increase in heart rate with nifedipine is inhibited by propanolol probably by inhibiting the cardiovascular effects of the activity of the sympathetic nervous system.

Incidence of pre-eclampsia in rural India varies from 7-10%.

Murakam et al (1972), Vedo et al (1979), Borlet et al (1983); it has also been tested in patients with hypertension. Most of the patients investigated until now had a normal renal function. Nifedipine has been used in only a few cases of hypertensive crises. We report here on our positive experience with the use of Nifedipine in 10 patients with a hypertensive crises and decreased renal function. Walters and Redman (1984) successfully used oral Nifedipine in 21 patients for acute severe hypertension in pregnancy or in puerperium.

A pilot study in 20 women with eclampsia and or SPIH revealed that sublingual nifedipine by 10 mg perforated capsule was an effective method of lowering blood pressure rapidly without any significant systemic side effects.

Nifedipine reduces both systolic and diastolic blood pressures with a minimal amount of side effects including orthostasis (Spurrell et al, 1974). Nifedipine also induces a powerful baroreceptor mediated reflex beta-adrenergic response to affect its negative ionotropic action and thus enhancing ventricular performance (Ellrodt et al, 1980). It suggests a state of tachycardia in the patients treated with nifedipine but in the present study the average pre-operative pulse rate was only 86.5±6.1. This did not cause any concern and the response at intubation was only a subduced like.

Reported side effects of nifedipine are hypotension, tachycardia and A.V. conduction blockage, none of which were present pre-operatively in the patient in this study.

Page and Christianson (1976) : Hypertension may coexist with pregnancy either as an essential hypertension or as a feature of pre-eclampsia. Severe hypertension during pregnancy is a major risk factor to both mother and the foetus. Hence it is imperative to institute antihypertensive therapy in such patients for successful continuation of pregnancy.

Redman (1977) : Among the antihypertensive agents, a methyldopa has been most commonly used for the treatment of pregnancy associated hypertension.

Stone et al (1980) have evaluated the efficacy of a single, oral or sublingual dose of nifedipine in preventing the rise in pulse and blood pressure induced by laryngoscopy and endotracheal intubation. Nifedipine exerts little or no effect on the blood pressure in normotensive subject. When given sublingually 10 mg nifedipine lowers blood pressure markedly, 15 minutes after its administration and the effect lasts for 90 minutes.

Kawajuna et al (1978), Aoki et al (1978) observed when nifedipine is administered orally or sublingually 90% of the drug is absorbed. The drug is detectable in the serum 3 minutes after the sublingual and 20 minutes after the oral administration on oral nifedipine (10 mg) exerts the peak haemodynamic effects

in 30-60 minutes which lasts for 6-10 hours.

Halothane has been shown to inhibit the slow calcium channel (Lynch et al, 1980) and this may cause myocardial depression (Merin and Pask, 1980) and vascular dilatation (Altura et al, 1980). Halothane may thus be expected to potentiate the effect of nifedipine and this has been substantiated in the present study.

Smith et al (1982) : In severe hypertension, hydralazine and diazoxide are employed but there are certain limitations associated with the use of these agents as they have to be administered parenterally and there is high incidence of side effects, the use of these agents at times it become extremely difficult to control hypertension in pregnancy with conventional antihypertensive drugs.

Rever et al (1982) oral nifedipine attenuated the pressure response only to a limited extent. It is likely that gastric absorption of nifedipine in the perioperative period was erratic and effective blood levels were not achieved. Sublingual nifedipine proved to be significantly more effective in checking the rise in mean arterial pressure. But nifedipine did not check the rise in pulse rate. This was probably because nifedipine is devoid of any effect on the A.V. nodal conduction. But despite this drawback in nifedipine, the rate pressure product, which is an index of myocardial O_2 demand remains lower in nifedipine treated subjects.

Murphy et al (1983) : Nifedipine, a calcium channel blockers, has been found to be effective and safe in patients having moderate to severe essential hypertension.

Huysman et al (1983) emphasized an advantage of a calcium antagonist in comparison to other vasodilators that it selectively increases cerebral and cardiac blood flow, as has been shown in human experiments they suggest that a short term use of nifedipine does not appear to compromise neonatal outcome.

Rubin et al (1984) studied nifedipine ... was found to be useful in hypertension in pregnancy and suggested that it may have a place in the treatment of hypertensive problems in pregnancy.

Jacob et al (1984) who found that duration of response lasted 3½ - 4 hours in non gravid patients.

Two hundred and sixty nine eclampsia and 681 SPIH patients admitted with sustained diastolic blood pressure (110 mm Hg)or higher or a systolic BP of 160 mm Hg or higher) to eclampsia room of Lady Hardinge Medical College and Hospital during 3 years period from January 1984 to December, 1986, comprised the study group. These patients were given lytic cocktail therapy or I/V diazepam or parenteral magnesium sulfate as first line anticonvulsant therapy.

Dulitzty et al (1986) and Martinelli et al (1986) have shown that nifedipine when used alone is effective and safe in pregnancy.

Jain et al (1987) : At present no other anti-hypertensive drug is available in India which can be effective in lowering the blood pressure in hypertensive emergencies during pregnancy within 30 minutes. Nifedipine can lower the blood pressure within 20 to 30 minutes and has no adverse effect on foetus. Therefore this drug can be useful additon to the armamentorium of anti-hypertensive drugs used in pregnancy.

Blood pressure is significantly lowered after sublingual administration of nifedipine in patients with uncontrolled hypertension presenting for caesarean section. The peak effect occurs in 20 minutes. The effect is sustained and the blood pressure remains stable throughout the period of anaesthesia. The blood pressure does not rise to alarming levels and even at the time of intubation or extubation. There is no significant change in pulse rate also. But Zusman et al (1987) reported a rise of 3.7 to 6.7% in pulse rate in nifedipine treated patients during anaesthesia and operation. The finding of our study confirm the observations reported by Zusman et al (1987) and Jain et al (1987).

Constantive et al (1987) have used slow release nifedipine with atenolol and alpha methyldopa in 23 hypertensive female and found this combination useful.

Lubbe (1987) reported that elucidation of some of the mechanism responsible for blood pressure elevation in pregnancy has permitted therapy to be based on more

rational principles. The decreased arterial reactivity encountered in normotensive pregnancy is most likely mediated by prostaglandins, preventive therapy using low dose aspirin is an option to prevent development of proteinuria in pre-existing hypertension and provide prophylaxis against pregnancy - induced hypertension.

2. Antihypertensive therapy utilizing sympathetic inhibition with either methyldopa or alpha and beta adrenoceptor blockade yield and the most promising results vasodilation with hydralazine, calcium entry blockers (nifedipine) intravenous labetalol or diazoxide is primarily used in severely hypertensive patients. The use of orally administered nifedipine in severely hypertensive women is associated with encouraging results.

3. It is clear that women with blood pressure levels greater than 170/110 mm Hg need antihypertensive therapy for maternal safety. It remains to be proven to what extent foetal growth and welfare can be improved in women with diastolic pressure levels 85 - 110 mm Hg when adrenoceptor blocking agents and used for blood pressure control. Initial studies are suggestive of improved foetal growth, prevention of proteinuria and the respiratory distress syndrome but more long term controlled studies are required.

4. In a recent study, at our institution, of foetal growth during long term antihypertensive therapy treatment with pindolol yielded better foetal growth

than therapy with atenolol. It is as yet unclear whether the ISA or beta$_2$ mediated vasodilation associated with pindolol was responsible for the improved foetal growth. Further controlled studies are indicated in hypertension in pregnancy to confirm the suggested benefits of beta adrenoceptor blocker therapy.

Constantine et al (1987) : Slow release nifedipine has been used in the treatment of severe hypertension in 23 pregnant women. In 22 this was in combination with other drugs, in 18 including atenolol. Good control of blood pressure was achieved in 20 women. The perinatal mortality of the group was 130/100 with a high caesarean section rate (71% of live births) a high rate of abnormal OTGS, a high rate of premature delivery and a high rate of infarcts who were small for dates. Whether this is due to the disease process or the medication is uncertain. For the present time these combinations should only be used in severe hypertensive or in the context of a controlled trial.

Ebeigbe et al (1987) : The effect of Bay K 8644, a dihydropyridine Ca^{2+} agonist, on in vitro contractile response and of inferior epigastric arteries from normotensive (N) and pre-eclamptic (P) subjects has been investigated, with a view to further defining the mechanism of the increased vascular sensitivity associated with pregnancy - induced hypertension. Bay K 8644 - 10(10)-10)-7) M - caused dose dependent

contractions of M as well as P arteries under resting conditions in the order : P greater than N and caused development of rhythmic contractions in both N and P arteries. Bay K 8644 effects were prevented by 3X10(-8) M. Nifedipine (Ca^{+2} antagonist). Bay K 8444 also significantly ($p < 0.05$) enhanced the sensitivity as well as maximal contractile responses to CaC_{12} in 40 MMK^{+-} depolarized Ca depleted N and P arteries in the order P greater than M. The results suggest that the increased peripheral vascular sensitivity associated with pregnancy induced hypertension may be due to least in part, to enhanced activity of the potential sensitive Ca^{2+} channels in arterial smooth muscle plasmalemma.

Ahokas et al (1988) studied the short term effect of the calcium channel blocker, nifedipine on maternal hemodynamics and organ perfusion in 12 hypertensive spontaneously pregnant rats by mean of the radioactive labelled microsphere technique. The normal fall in blood pressure during pregnancy was prevented by reducing little size to two conceptuses on day 7 of gestation. Nifedipine (200 micrograms/kg) effectively lowered mean arterial pressure 25% by decreasing total peripheral resistance 38% (cardiac output was increased 15%). Blood flows to the splanchnic region and the reproductive organs were increased after nifedipine administration. The increase in blood flow to the reproductive organs was the result of increased ovarian and uterine wall perfusion blood flow

was not significantly altered, but resistance was decreased. Thus, the use of nifedipine to lower maternal blood pressure in pregnancy complicated by extreme hypertension does not necessarily decrease uteroplacental blood flow.

Lindow et al (1988) studied the effect of nifedipine on uteroplacental blood flow in nine hypertensive women in the trimester of pregnancy and compared with the effects of a placebo in nine similar hypertensive women. An index of uteroplacental blood flow was observed twice before treatment and once after treatment, by measuring the increase in radioactivity in the region of the placenta with a gamma camera following an intravenous injection of Indium 113 ml. There was no significant change in the blood flow index in either the nifedipine or the placebo. Treated groups despite a significant fall in the blood pressure with nifedipine. Nifedipine lowers the blood pressure without any apparent reduction in uteroplacental blood flow.

The effect of Nifedipine (Adalat, Bayes Miles) a calcium channel blocker, which has a well established place in non-obstetric hypertension was compared with dihydralazine in 33 primigravidas with severe hypertension of pregnancy. Patients with a diastolic blood pressure greater than 110 mm Hg before drug administration were randomly assigned to treatment with either nifedipine or dihydralazine. Both drugs were found to be equally

efficacious. Nifedipine, however, showed an earlier onset of action in lowering systolic blood pressure and had the advantage of oral administration (Seabe and Moodley et al, 1989).

Lurie and Fenabel et al (1990) studied the effect of lowering the maternal blood pressure with sublingual nifedipine on the fetal heart rate in 51 patients with severe pregnancy induced hypertension. No fetal heart rate abnormalities were observed while achieving an excellent control of blood pressure.

Hypertensive diseases of pregnancy are clinically important because they can adversely influence the health and life of both mother and baby. Hypertensive disease is the commonest cause of maternal mortality in England and Wales accounting for 20.4% of maternal deaths. It is depressing to note that most if not all of these deaths are preventable. Three broadly different kinds of hypertension can be identified as potential complications of pregnancy. Chronic hypertension, pregnancy induced hypertension and pre-eclampsia. Where chronic hypertension is treated with methyldopa and PIH is treated with Atenolol, there is evidence that therapy is beneficial in terms of immediate pregnancy outcome and is not harmful to the child. Atenolol is currently being evaluated in combination with nifedipine to treat cases of early onset of severe pre-eclampsia and preliminary results are encouraging prevention rather than cure

should be the aim in managing hypertensive diseases during pregnancy. Early intervention can prevent serious problems later on (Rubin, 1990).

Manninen et al (1990) studied the effect of nifedipine on blood pressure, plasma renin activity and calcium metabolism in nine hypertensive pregnant patients. Nifedipine (10 mg thrice daily per Os) reduced blood pressure from 158/103 ± 4/1 to 150/96 ± 4/2 mm Hg (mean ± 8 cm) during 4 to 5 days treatment (p less than 0.05). The percentage change in diastolic blood pressure correlated negatively with the initial ambulatory(p $<$0.001) rest (p $<$0.01) plasma renin activity and the initial daily urine calcium excretion (p $<$0.01) calcium excretion in urine correlated positively with the initial ambulatory and rest plasma renin activity (p $<$0.01). The blood pressure reduction did not correlate with serum ionized or total calcium or the initial blood pressure. In six non pregnant women, the rest plasma renin activity increased (p $<$0.05) after four days administration of nifedipine. In the patients with hypertensive pregnancy. No changes in plasma renin activity were found during the treatment. The results indicated that the initial plasma renin activity, but neither the serum ionized calcium nor the initial blood pressure predicted the blood pressure, lowering effect of nifedipine in hypertensive pregnancy.

Campanacei et al (1990) showed that hypertension complicates approximately 10% of all pregnancies and

accounts for 20% of all the maternal deaths. Blood pressure normally decreases in the first trimester of pregnancy, secondary to a decrease in peripheral vascular resistance reaches its lowest point in the second trimester and then gradually increases to or near pregravid levels at term. Normal pregnant women develop vascular resistance to the pressure effect of angiotensin II which is precociously lost in women who develop gestational hypertension. Prostaglandins seem to be involved in the development of this vascular refractoriness. An acute and reversible lesion defined "Glomerular endotheliosis has been described as the basic pathologic pattern of pre-eclamptic nephropathy, although gestational hypertension can be superimposed on undiagnosed essential hypertension or any of a variety of renal diseases. The primary goal when treating gestational hypertension is successful termination of the pregnancy with the least trauma to mother and fetus. Antihypertensive drugs could be administered to prolong pregnancy when this is considered desirable, although pharmacological therapy of gestational hypertension remains a subject for dispute, because of the lack of closely controlled studies. Hydralazine and methyldopa are drugs with a long history of use in gestational hypertension beta-blockers have been shown to be as effective as methyldopa. Clinical experience with nifedipine is limited but controlled clinical trials, currently in progress, suggest its suitability.

Luque Otero et al (1990) postulated that mild hypertension is very common, 50% of hypertensive being with their diastolic blood pressure between 90 and 104 mm Hg. Many large studies especially HDFD had shown not only the deleterious cardiovascular effects of mild hypertension but also the benefits obtained with the therapy. The non pharmacological approach should be the first step in the treatment of mild hypertension. Isolated systolic hypertension have a high prevalence in the elderly increasing the cardiovascular morbidity and mortality. Sodium restriction and if necessary, vasodilators increasing the arterial compliance seem to be the logical approach to treat isolated systolic hypertension. Finally eclampsia is the most serious complication of pregnancy induced hypertension. The treatment with bed rest and either beta blockers or methyldopa is beneficial If eclampsia occurs hydralazine, magnesium sulphate or nifedipine should be used.

Pirhonen (1990) described the short term effect of 20 mg of oral nifedipine on maternal and fetal haemodynamics was investigated in 12 women with pregnancy induced hypertension. Within an hour after nifedipine, the mean arterial blood pressure fill by 17% and there was a slight increase in maternal heart rate. There was also a decrease in the systolic/diastolic (S/D) ratio in the flow velocity wave form in the uterine artery in

seven subjects , whereas the S/D ratio was unaffected in five subjects. Lack of change in the S/D ratio was associated with a less optimal pregnancy outcome. The neonates were delivered earlier, the rate of caesarean delivery was higher and the newborns were smaller. No changes were observed in the fetal heart rate pattern or in the umbilical or middle cerebral artery flow velocity wave forms after nifedipine in hypertensive pregnancies.

Puzey et al (1991) described the effect of nifedipine 5 mg administered sublingually to pregnant hypertensive patients was examined in a randomized controlled double blind study. The effect on maternal blood pressure and the fetal umbilical artery Dopples wave form was studied for 30 minutes before and 30 minutes after administration of the drug or placebo. This dose resulted in a significant drop in maternal blood pressure 30 minutes after administration and did not result in a significant change in the Doppler umbilical artery wave form (in fetuses with normal waveforms) when compared with a control group.

Remuzzi et al (1991) studied prevention and treatment of pregnancy associated hypertension in the last 10 years. High blood pressure complicates approximately 10% of all pregnancies. Hypertension in pregnancy falls into four categories (1) Pre-eclampsia - eclampsia, (2) Chronic hypertension of whatever cause, (3) pre-eclampsia-eclampsia superimposed to chronic hypertension or renal disease and (4) transient or late hypertension

(gestational hypertension). Pre-eclampsia, the association of hypertension, proteinuria and edema, accounts for more than 50% of all the hypertensive disorders of pregnancy and is a major cause of foetal and maternal morbidity and mortality. Distinguishing between pre-eclampsia and other causes of hypertension on clinical grounds can be difficult because of the lack of specific tests for differential diagnosis. Increased vascular resistance has been claimed as the primary cause of pre-eclampsia, however, a variable haemodynamic profile with relatively high cardiac output, normal filling pressure and inappropriately high systemic vascular resistances is now reported by most investigators. Imnalance between vasodilator and vasoconstrictor eicosanoids may account for platelets activation and increased responsiveness to pressure peptides. Altered prostacyclin (PGI_2) to thromboxane A_2 (TXA_2) ratio in maternal uteroplacental vascular bed may favour local platelets activation and vasoconstriction contributing to placental insufficiency and foetal distress. Alterna tively recent evidence seems to suggest that foetal placental circulation may be the site of the primary vascular injury. Whether low dose aspirin prevents pre-eclampsia because it inhibits the excessive maternal TXA_2 or whether the partial inhibition of foetal TXA_2 is also of therapeutic value remains to be established.

Treatment of severe hypertension in pregnancy is probably important to prevent cardiac failure or cerebr0vascular accidents in the mother. The need for pharmacological therapy of mild to moderate hypertension is still debaled, since no formal studies are available to clarify whether pharmacological treatment in such instances effectively reduces maternal or fetal risks. For the treatment of pre-eclampsia, hydralazine and nifedipine may be used when delivery is not applicable Labetalol and diazoxide are effective for hypertensive emergencies. Life threatening hypertension that does not respond to more conventional therapy is an indication for the use of sodium nitropruside. For chronic hypertension alpha methyldopa remains the treatment of choice, if ineffective hydralazine or beta-blockers are suitable Effectiveness and safety of other molecules remain elusive.

Fairlie et al (1991) early studies suggested that Doppler ultrasound held great promise as a non invasive, repeatable, and simple method of predicting hypertension in pregnancy and identifying those hypertensive pregnancies at high risk of maternal and fetal complications. Further studies have tempered this early enthusiasm by revealing the multiplicity of factors that may influence the Doppler waveform pattern. This makes interpretation of changes in the FVIN pattern difficult

Despite these difficulties there is evidence to suggest that Doppler velocimetry may contribute to two aspects of the management of hypertensive pregnancies. First, as a non-invasive method of investigating the effect of pharmacologic agents on maternal, foetal and placental circulation. Second, a number of studies support a useful role for Doppler, ultrasound measurement in the assessment of fetal well being in hypertensive complications. Foetal monitoring tests or be capable of indicating the optimum time for delivery. It does, however, appear to be a useful adjuvant in assessing the risk of perinatal complications especially in hypertensive pregnancies presenting before 30 weeks gestation.

Barton et al (1992) studied the pharmacologic and pharmacodynamic parameters of oral nifedipine in the immediate post partum period in eight women with pre-eclampsia. Peak serum concentrations of 18±2.1 micrograms/l occurred 40 minutes after ingestion of nifedipine (10 mg). The terminal elimination half life (mean : 1.35±0.3 hour) was found to be shorter than that reported for normotensive volunteers or non pregnant hypertensive women (Mean - 3.4±0.4 hours). A mean apparent oral elimination clearance of 3.8±1.3 ; l/hr/kg was more rapid than that found in normal volunteers (mean 0.49±0.09 l/hr/kg) or in women with pregnancy induced hypertension in the third trimester (mean 2.0±0.08 l/hr/kg). Initial radirs in mean arterial pressure were noted at 50 minutes

after ingestion of nifedipine, with an average reduction in mean arterial pressure of 13.8 mm Hg. A dosing interval of every 3 to 4 hours is suggested when rapid release nifedipine is used in the post partum patient with pre-eclampsia.

Manninen et al (1991) : Renal prostanoid excretion was investigated in nine hypertensive pregnancy patients before and during treatment with nifedipine 10 mg orally. Urinary excretion of prosticyclin (measured as 6-betaprostaglandin FI alpha, 6 keto-PGFI alpha) increased by 77% during nifedipine treatment ($p < 0.05$). No changes were found in prostaglandin E_2 (PGE_2) and thromboxane A_2 (as thromboxane B_2, TXB_2), excretion. A significant reduction in blood pressure did not correlate with an increase in 6-beto-PGFI alpha excretion. Plasma prekallikodin and urinary kallibrein and catecholamine excretions remained unaltered. In six normotensive nonpregnant women, increase in 6-beto-PGFI alpha, excretion during nifedipine treatment was not significant. No changes in PGE_2 and TXB_2 excretion were found whereas plasma prekallibrein was reduced ($p < 0.05$) and urinary excretion of kallibrein ($p < 0.05$) and noradrenaline ($p = 0.06$) increased under nifedipine. The results suggest that nifedipine enhances the renal 6-beta-PGFI alpha excretion in hypertensive pregnancy.

MATERIAL AND METHODS

MATERIAL AND METHODS

This study was conducted in the department of Anaesthesiology, M.L.B. Medical College, Hospital, Jhansi in 90 patients of age group between 19-30 years. All patients undergoing emergency caesarean section were included in the study. They were operated under general anaesthesia or spinal anaesthesia. Patients having systolic blood pressure above 140 mm Hg and diastolic above 90 mm Hg were included in the study. An informed consent was obtained from all patients.

All parturients who were undergo emergency caesarean section were subjected to detailed pre-anaesthetic check up half an hour before surgery. All patients were asked the history of oral intake, if the patient was starving and if time permits half an hour before surgery 0.6 mg Atropine sulphate was given intramuscularly. If there was history of oral intake then gastric tube was passed and gastric suction was done.

On arrival in operation theatre, blood pressure & heart rate were recorded in each patient.

Depending on the drugs used for the study the total number of 90 patients were divided into three groups.

GROUP I

This group consisted of 40 patients who were given sedation 10 mg diazepam intramuscularly half an

hour before the induction of anaesthesia.

GROUP II

This group also consisted of 40 patients who were given Nifedipine 10 mg sublingually half an hour before induction of anaesthesia.

Group I and II were further divided into group Ia & Ib and IIa & IIb as per the technique of anaesthesia applied. In group Ia and IIa general anaesthesia was given and in Ib and IIb spinal anaesthesia was given.

GROUP III

This group comprised of 10 patients who had severe hypertension with oedema and albuminuria. These were given diazepam 10 mg intramuscularly and Nifedipine 10 mg sublingually.

The patients of this group were operated under general anaesthesia (Nifedipine) capsule was cut at one end and the drug was administered sublingually half an hour before induction of anaesthesia.

MONITORING

Pulse rate, respiratory rate, blood pressure were recorded at :

1. the time of administration of Nifedipine.
2. 10 minutes after Nifedipine.
3. 20 minutes after Nifedipine.

4. 30 minutes after Nifedipine.
5. Just after endotracheal intubation.
6. 45 minutes after Nifedipine.
7. at the time of extubation.

TECHNIQUE OF ANAESTHESIA

Detailed of technique in each group is as follows :

I. General Anaesthesia with controlled Ventilation

All patients were in supine position on an operation table with a pillow under the occiput blood pressure and pulse rate were recorded. Intravenous drip of 5% dextrose or isotonic solution was started.

Pre-oxygenation was done for 3-4 minutes to all patients and during this time skin preparation and drapping was completed by obstetrician. Induction was done with a dose of thiopentone sodium 2.5% sclution in doses of 4-5 mg/kg body weight. This was followed by suxamethonium in doses of 1.5 mg to 2.0 mg/kg body weight about 100 mg was loaded and given intubation with a cuffed endotracheal tube was smoothly and swiftly carried out following which the operation started. The cuff of the endotracheal tube was then promptly inflated ensuring the aeration chest expansion equal on both sides. Anaesthesia was maintained with Nitrous oxide and oxygen (5.5 litre per minutes) and intermittent positive pressure ventilation using Margills circuit. In most of

the patients the initial dose of suxamethonium provided sufficient relaxation till the foetus was delivered. Once the spontaneous ventilation starts suxamethonium was used in doses of 10 mg subsequently till the surgery was over. After a delivery of the infant fortwin 10-20 mg and phenargan 25 mg intravenously was used to eleviate pain and awareness.

II. Subarachnoid Block

Blood pressure and pulse rate were recorded before the start of the procedure. Intravenous drip started with fast infusion of 5% dextrose followed by normal saline/Ringerlactate 540 ml. Patient was put on left lateral position with spines flexed. Area was cleaned thoroughly and a skin wheal raised with the injection of lignocaine 1% solution in L_3-L_4 interspinous space. For spinal injection a 20 S.W.G. needle was mostly used. When tip of needle enters into the sub-arachanoid space a free flow of C.S.F. is observed. Bupivacaine (Sensorcaine heavy) in doses 1.5-2.0 ml (10 mg) was injected or 5% lignocaine (0.8 to 1.0 ml). Then patient was made supine. Another 900 ml of Ringer lactate or 540 ml of normal saline was infused rapidly. After the injection of spinal block and lateral tilt of table the surgeon was asked to commence the operation. Pulse rate and blood pressure were recorded till the delivery of the infant and also after delivery. Injection

ergometrine was given intravenously after delivery of the foetus along with oxytocin in infusion bottle.

O B S E R V A T I O N S

OBSERVATIONS

The study was conducted in 90 patients of age group between 19 - 30 years. The patients were randomly divided into three groups. Group I and II contained 40 patients each and group III contained 10 patients only. Group I and II were further divided into subgroups Ia & Ib and IIa & IIb. There were 20 patients in each subgroup. The mean age, parity, period of gestation in each group are shown in table I.

TABLE I : Showing maternal age, parity and period of gestation (Mean, Range).

Parameters	Group I		Group II		Group
	Ia	Ib	IIa	IIb	III
Maternal age (years)					
Mean	22.50	22.00	26.00	23.30	21.70
Range	(19-30)	(19-25)	(22-30)	(20-29)	(20-25)
Parity					
Mean	1.7	2.0	1.7	1.7	2.6
Range	(1-4)	(1-3)	(1-4)	(1-3)	(1-5)
Period of gestation (weeks)					
Mean	39-00	38.00	39.00	39.20	38.90
Range	(37-42)	(37-41)	(37-42)	(38-40)	(37-40)

PIE CHART SHOWING MEAN MATERNAL AGE IN VARIOUS GROUPS

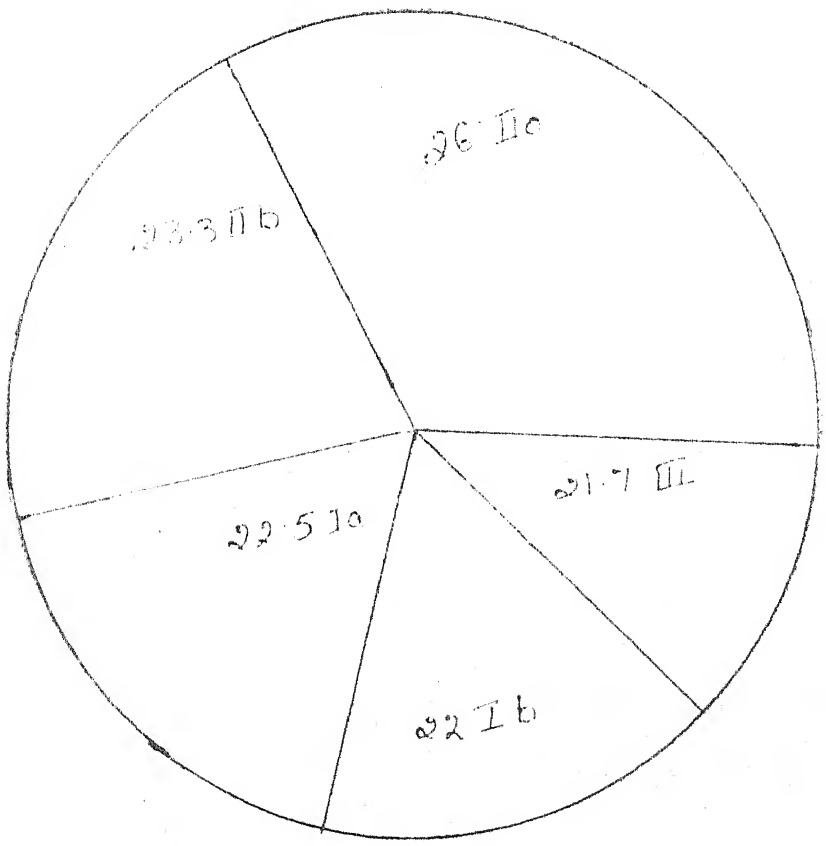


TABLE II : Showing drugs and procedure used in different groups

Groups	Subgroups	No.of cases	Drug and anaesthetic procedure
I	Ia	20	Diazepam 10 mg GA with controlled ventilation
I	Ib	20	Diazepam 10 mg spinal analgesia.
II	IIa	20	Nifedipine 10 mg + GA with controlled ventilation.
II	IIb	20	Nifedipine 10 mg + spinal analgesia.
III		10	Nifedipine 10 mg + Diazepam 10 mg with GA with controlled ventilation.

TABLE III : Showing the changes in pulse rate, blood pressure in subgroup Ia(Mean±SD,Range).

Parameters	Time of observation						
	Initial	10 minutes after diazepam	20 minutes after diazepam	30 minutes after diazepam	Just after intubation	45 minutes after diazepam	At the time of extubation
Pulse rate/min	96.50 ± 6.30	84.60 ± 8.80	94.50 ± 6.10	93.90 ± 6.06	93.70 ± 5.09	92.90 ± 5.06	92.40 ± 5.16
	(104-80)	(102-80)	(102-80)	(102-82)	(98-82)	(96-84)	(98-82)
Systolic BP mm Hg	150.32 ±8.554	131.48 ±5.690	121.68 ±4.095	124.82 ±4.805	135.73 ± 5.12	126.40 ± 4.67	130.06 ± 4.43
	(172-140)	(140-120)	(130-110)	(130-112)	(140-122)	(136-118)	(140-120)
Diastolic BP mm Hg	99.60 ± 4.00	84.00 ± 3.09	79.60 ±2.154	82.19 ± 3.18	85.80 ± 3.18	94.20 ± 4.10	84.80 ± 3.96
	(112-92)	(90-80)	(86-72)	(88-86)	(90-82)	(88-78)	(90-80)
Mean arterial pressure	124.50 ±34.05	107.70 ±37.70	100.60 ±32.40	103.50 ±32.60	110.50 ±33.20	105.30 ±32.20	107.40 ±33.60
	(138-124)	(138-120)	(130-122)	(130-120)	(128-120)	(126-100)	(128-100)

TABLE IV : Showing the changes in pulse rate, blood pressure in subgroup Ib.

Parameters	Time of observation						
	Initial	10 minutes after diazepam	20minutes after diazepam	30 minutes after diazepam	Just after intubation	45 minutes after diazepam	At the time of extubation
Pulse rate/min.	99.70 ±1.10 (104-92)	100.20 ± 8.78 (102-90)	98.70 ± 5.02 (102-90)	101.40 ± 3.48 (98-90)	100.50 ± 4.91 (100-90)	106.20 ± 3.03 (98-86)	101.01 ± 2.90 (98-86)
Systolic BP mm Hg	152.32 ± 8.66 (172-140)	150.00 ± 8.40 (150-120)	131.48 ± 5.60 (140-120)	120.60 ± 4.21 (132-110)	124.00 ± 8.80 (130-112)	135.70 ± 5.12 (140-122)	126.40 ± 4.60 (136-118)
Diastolic BP mm Hg	100.00 ± 4.20 (112-92)	99.40 ± 4.00 (112-92)	84.00 ± 3.20 (90-80)	79.80 ± 2.14 (86-72)	82.19 ± 3.18 (88-86)	95.20 ± 3.18 (90-82)	84.20 ± 4.10 (88-72)
Mean arterial pressure	126.10 ±30.02 (136-128)	107.70 ±28.10 (124-120)	100.80 ±28.20 (120-110)	104.50 ±30.20 (124-104)	110.50 ±29.20 (126-106)	105.30 ±28.40 (126-104)	107.40 ±27.20 (120-102)

TABLE V : Showing the changes in pulse rate and blood pressure in subgroup IIa.

Parameters	Time of observation						
	Initial	10 minutes after nifedipine	20 minutes after nifedipine	30 minutes after Nifedipine	just after intubation	45 minutes after nifedipine	At the time of extubation
Pulse rate/min.	96.30 ± 9.83 (104-80)	95.90 ± 9.03 (102-80)	95.90 ± 9.80 (100-80)	94.30 ± 7.9 (98-80)	94.60 ± 8.00 (98-82)	94.40 ± 9.92 (98-82)	94.90 ± 9.23 (98-80)
Systolic BP mm Hg	134.00 ± 8.58 (174-138)	134.40 ± 5.80 (142-122)	122.68 ± 4.80 (130-110)	126.84 ± 4.90 (130-112)	135.73 ± 5.40 (140-122)	128.40 ± 4.80 (138-118)	130.08 ± 4.60 (140-118)
Diastolic BP mm Hg	99.60 ± 4.00 (112-92)	84.00 ± 3.90 (90-80)	80.10 ± 2.20 (86-72)	82.19 ± 3.18 (88-84)	85.80 ± 3.20 (90-84)	84.20 ± 4.20 (88-80)	84.80 ± 3.80 (90-80)
Mean arterial pressure	126.50 ±35.00 (138-124)	107.90 ±32.80 (136-118)	100.40 ±33.40 (130-120)	103.40 ±32.40 (130-118)	110.50 ±33.20 (128-120)	105.40 ±31.80 (126-102)	107.60 ±33.80 (128-100)

TABLE VI : Showing the changes in pulse rate and blood pressure in subgroup IIb.

Parameters	Time of observation						
	Initial	10 minutes after nifedipine	20 minutes after nifedipine	30 minutes after nifedipine	Just after intubation	45 minutes after nifedipine	At the time of extubation
Pulse rate/min	99.80 ± 1.20	99.80 ± 8.70	105.80 ± 8.08	105.00 ± 8.46	104.80 ± 8.04	100.40 ± 8.04	100.20 ± 8.20
	(104-92)	(102-90)	(104-92)	(98-86)	(98-82)	(98-82)	(100-84)
Systolic BP mm Hg	154.00 ± 8.20	134.00 ± 5.20	123.41 ± 4.80	126.84 ± 4.90	135.73 ± 5.40	130.40 ± 4.20	130.20 ± 4.20
	(170-138)	(142-122)	(130-110)	(130-112)	(140-122)	(138-118)	(140-118)
Diastolic BP mm Hg	99.60 ± 4.00	84.00 ± 3.09	80.40 ± 2.20	82.19 ± 3.18	85.80 ± 3.20	86.20 ± 4.40	84.80 ± 3.40
	(114-92)	(94-80)	(86-72)	(88-84)	(92-84)	(86-80)	(92-80)
Mean arterial pressure	126.50 ±35.20	108.90 ±32.80	100.20 ±33.40	104.40 ±32.40	112.50 ±34.20	106.40 ±31.20	108.20 ±32.80
	(138-124)	(136-118)	(132-120)	(130-118)	(128-120)	(128-102)	(130-100)

TABLE VII : Showing the changes in pulse rate and blood pressure in group III.

Parameters	Time of observation						
	Initial	10 minutes after diazepam + nifedipine	20 minutes after diazepam+ nifedipine	30 minutes after diazepam+ Nifedipine	Just after intubation	45 minutes after diazepam+ nifedipine	At the time of extubarion
Pulse rate/min	102.80 ±10.32	103.00 ± 9.67	100.80 ± 6.41	101.80 ± 6.40	104.20 ± 6.66	103.80 ± 8.60	100.40 ± 8.89
	(108-100)	(108-98)	(104-98)	(102-98)	(100-98)	(102-98)	(100-96)
Systolic BP mm Hg	160.32 ± 9.55	141.48 ± 6.69	131.68 ± 5.00	134.82 ± 5.80	145.73 ± 6.12	136.40 ± 5.60	140.06 ± 5.40
	(180-140)	(144-120)	(134-110)	(134-112)	(150-122)	(146-118)	(140-126)
Diastolic BP mm Hg	104.60 ± 5.00	94.00 ± 4.20	89.60 ± 3.10	84.82 ± 4.10	88.80 ± 4.10	86.20 ± 4.40	84.80 ± 4.20
	(116-94)	(94-80)	(88-74)	(90-86)	(92-86)	(92-78)	(92-82)
Mean arterial pressure	136.50 ±35.00	117.90 ±34.80	110.40 ±33.40	113.40 ±32.40	120.50 ±33.20	115.40 ±31.80	117.60 ±33.80
	(140-124)	(138-118)	(134-120)	(132-118)	(128-118)	(128-102)	(130-100)

TABLE VIII : Statistical comparison of group Ia and IIa.

		Time of observation						
		Initial	10 minutes after drug	20 minutes after drug	30 minutes after drug	Just after intubation	45 minutes after drug	At the time of extubation
Pulse rate	't'	1.9	1.9	2.0	2.2	2.9	3.6	8.3
	p	>0.05	>0.05	<0.05*	<0.05*	>0.05	>0.05	<0.01**
Systolic B.P.	't'	1.34	1.42	2.6	2.9	2.7	3.3	2.9
	p	>0.05	>0.05	<0.05*	<0.01**	<0.05*	<0.01**	<0.01**
Diastolic B.P.	't'	1.10	1.20	2.10	2.6	2.9	2.7	3.6
	p	>0.05	>0.05	<0.05*	<0.05*	<0.01**	<0.05*	<0.001**
Mean arterial pressure	't'	0.9	0.8	0.74	-	0.93	1.0	0.6
	p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

$n_1 + n_2 - 2 = 38$, d.f. = 38

* Significant ** Highly significant.

TABLE IX : Statistical comparison of group Ib and IIb.

		Time of observation						
		Initial	10 minutes after drug	20 minutes after drug	30 minutes after drug	Just after intubation	45 minutes after drug	At the time of extubation
Pulse rate	't'	1.6	1.9	2.1	2.2	3.3	2.9	3.6
	p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Systolic BP	't'	-	1.7	2.0	2.4	2.6	3.1	2.7
	p	-	>0.05	<0.05*	<0.05*	<0.05*	<0.01**	<0.01**
Diastolic BP	't'	1.9	2.8	3.5	3.6	5.3	4.4	3.7
	p	>0.05	<0.01**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**
Mean arterial pressure	't'	1.3	0.9	0.8	1.5	0.7	0.6	-
	p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	-

d.f. = 38, * Significant ** Highly significant.

TABLE X : Statistical comparison of group Ia and III.

		Time of observation						
		Initial	10 minutes after drug	20 minutes after drug	30 minutes after drug	Just after intubation	45 minutes after drug	At the time of extubation
Pulse rate	't'	1.26	1.66	2.6	1.29	1.33	1.28	1.25
	p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Systolic BP	't'	1.34	1.67	2.6	2.8	3.6	3.4	2.7
	p	>0.05	>0.05	<0.05*	<0.01**	<0.01**	<0.01**	<0.05*
Diastolic BP	't'	0.14	2.2	2.16	2.63	2.7	2.8	3.41
	p	>0.05	<0.05*	<0.05*	<0.05*	<0.05*	<0.01**	<0.001**
Mean arterial pressure	't'	0.14	0.009	0.13	0.05	-	0.21	0.01
	p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

d.f. = 28 * Significant ** Highly significant.

TABLE XI : Statistical analysis of group IIa and III.

		Time of observation						
		Initial	10 minutes after drug	20 minutes after drug	30 minutes after drug	Just after intubation	45 minutes after drug	At the time of extubation
Pulse rate	't'	1.22	1.21	1.45	1.36	1.28	1.22	1.36
	p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Systolic BP	't'	1.4	1.2	2.2	2.7	3.4	2.9	2.6
	p	>0.05	>0.05	<0.05*	<0.05*	<0.01**	<0.01**	<0.05*
Diastolic BP	't'	3.0	2.34	2.4	2.6	3.6	4.6	4.3
	p	<0.01**	<0.05*	<0.05*	<0.05*	<0.01**	<0.001**	<0.001**
Mean arterial pressure	't'	1.02	0.45	0.11	0.016	0.20	-	-
	p	>0.05	>0.05	>0.05	>0.05	>0.05	-	-

d.f. = 28, * significant, ** Highly significant.

PULSE RATE

Table III, IV, V, VI and VII show the changes in pulse rate in all the groups recorded at various time interval. Mean basal pulse rate of any group was not significantly different. There was a significantly decrease in pulse rate in group Ia and IIa after premedicant and there was also significantly increase in pulse rate in group Ib, IIb and III after premedication recorded at :

i) the time of premedicant.
ii) 10 minutes after premedicant.
iii) 20 minutes after premedicant.
iv) 30 minutes after premedicant.
v) just after endotracheal intubation.
vi) 45 minutes after premedicant.
vii) at the time of extubation.

After premedicant there was a further decrease in pulse rate in group Ia and IIa. The maximum decrease in pulse in group Ia and IIa was 92.90±7.06 beats/minute after 45 minutes of diazepam, 94.30±7.9 beats/minute after 30 minutes of nifedipine. The effect came 15 minutes earlier in group IIa than Ia.

After premedicant there was further increase in pulse rate in group Ib, IIb and III. The maximum increase in pulse rate in group Ib was 101.4±2.48 beats/minute at 30 minutes after diazepam, and in group IIb it was 105.60±8.46 beats/minute at 20 minutes after nifedipine and in group III it was 104.20±6.6 beats/minute

just after intubation. The maximum increase in pulse rate was in group IIb that was 105.60±8.4 and effect came at 10 minutes earlier than the group Ib but this difference was quite insignificant ($p > 0.05$).

SYSTOLIC BLOOD PRESSURE

Table III, IV, V, VI and VII show the changes in systolic blood pressure in group Ia, Ib, IIa, IIb and III recorded at various time intervals. Mean basal systolic blood pressure of any group was not significantly differed. There was a significant decrease in systolic blood pressure in all groups after atropine, diazepam, nifedipine and diazepam-nifedipine combination premedication recorded at :

i) the time of premedicant.
ii) 10 minutes after premedicant.
iii) 20 minutes after premedicant.
iv) 30 minutes after premedicant.
v) just after endotracheal intubation.
vi) 45 minutes after premedicant.
vii) at the time of extubation.

After premedicant there was a further decrease in pulse rate in all three groups. Following laryngoscopy and intubation systolic blood pressure decreased very significantly in all groups reaching a maximum reduction at 20-30 minutes after premedicants and decreased gradually over the next 15 minutes. Only in

group II and III the maximum recorded systolic blood pressure was more than that of group I but this difference was quite insignificant ($p > 0.05$). In group II and III the systolic blood pressure decreased maximally at 30 minutes after premedicant but even in these groups it was significantly lesser in basal values ($p < 0.01$).

DIASTOLIC BLOOD PRESSURE

Table III, IV, V, VI and VII show the changes in diastolic blood pressure in all the groups recorded at various time intervals. Mean basal diastolic blood pressure of any group was not significantly different. There was a significant decrease in diastolic blood pressure in all groups after atropine, diazepam and diazepam-nifedipine combination premedication recorded at:

i) the time of premedicant.
ii) 10 minutes of premedicant.
iii) 20 minutes of premedicant.
iv) 30 minutes of premedicant.
v) just after endotracheal intubation.
vi) 45 minutes after premedicant.
vii) at the time of extubation.

After premedicant there was a further decrease in diastolic blood pressure in all three groups. Following laryngoscopy and intubation pulse rate decreased very significantly in Ia and IIa groups reaching a maximum reduction at 30 minutes after premedicants and decreased

gradually. Over the next 15 minutes, only in group II and III the maximum recorded diastolic blood pressure was more than that of group I but this difference was quite insignificant ($p > 0.05$). In group II and III the diastolic blood pressure decreased maximally at 20 minutes after premedicant but even in these groups at was significantly lesser the basal value.

MEAN ARTERIAL PRESSURE

Table III, IV, V, VI and VII show the mean arterial pressure in all the group recorded at various time intervals. The basal mean arterial pressure was not significantly different from each other. There was a decrease in mean arterial pressure after 30 minutes of premedicant in all groups. The mean arterial pressure decreased significantly in all groups ($p < 0.01$) after 10 minutes of premedicant and rose to a maximum at 20-30 minutes and then remained stationary. The maximum decrease in mean arterial pressure was significantly lesser in group I.

In all groups the mean arterial pressure remained lesser than the basal values, after 10 minutes the difference being statistically significant in group II and III.

On comparing the effect of diazepam with nifedipine during general anaesthesia in group Ia and IIa (Table VIII) it can be seen that :

1. Nifedipine produced a significant change in pulse rate 20 minutes after administration as compared to diazepam.
2. A significant difference of the effect on blood pressure (both systolic and diastolic) was noted between diazepam and nifedipine as early as 20 minutes after administration.
3. The mean arterial pressure however, remained fairly stationary.

On comparing the effect of diazepam with nifedipine during spinal analgesia in group Ib and IIb (Table IX), it can be seen that :-

1. Nifedipine produced a significant change in pulse rate 20 minutes after administration as compared to diazepam but statistically insignificant.
2. A significant difference of the effect on blood pressure (both systolic and diastolic) was noted between diazepam and nifedipine as early as 20 minutes after administration.
3. The mean arterial pressure however, remained fairly stationary and statistically insignificant($p > 0.05$).

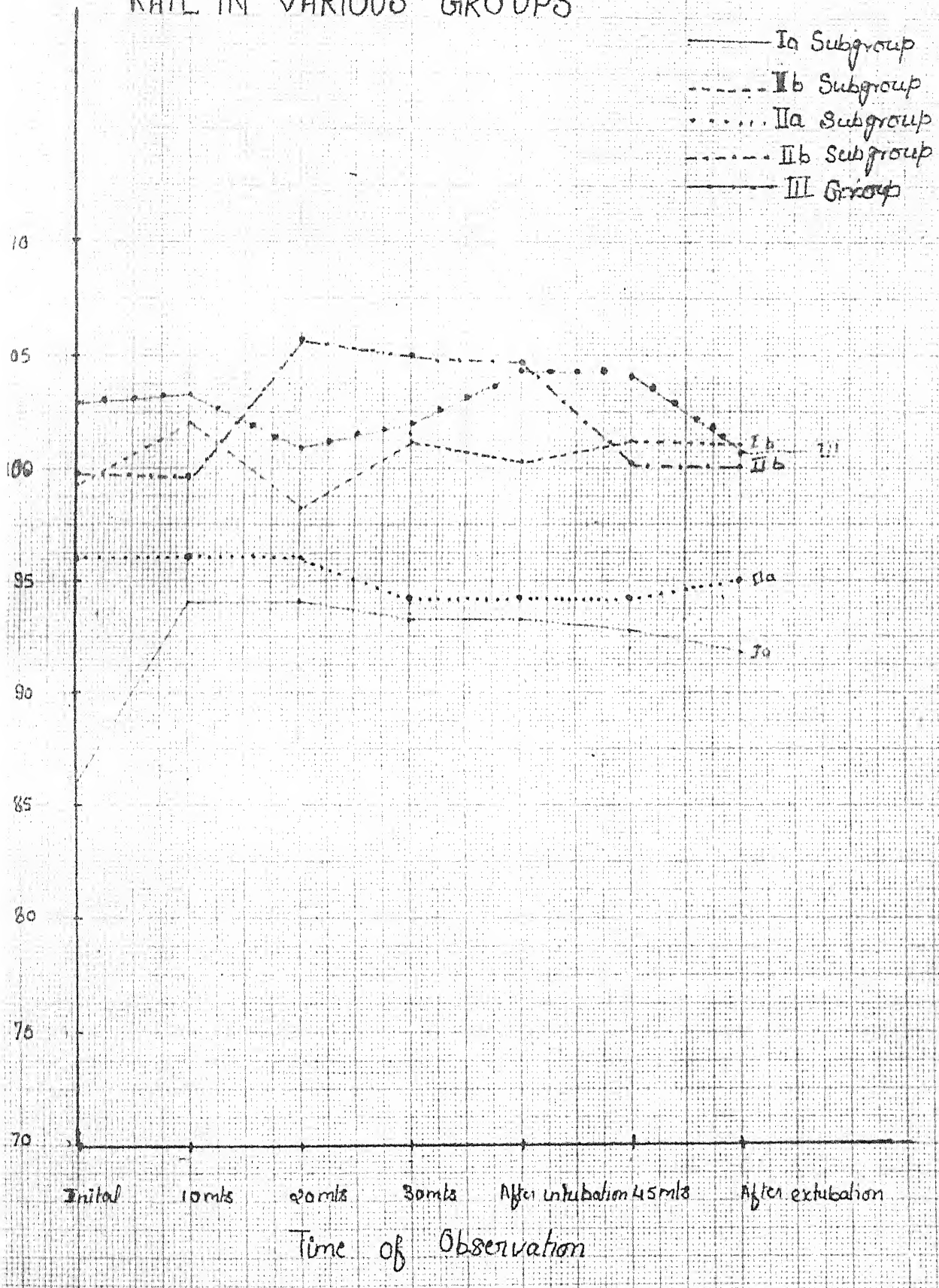
On comparing the effect of diazepam with nifedipine-diazepam combination during general anaesthesia with controlled ventilation in group Ia and III(Table X), it can be seen that :-

1. Nifedipine-diazepam combination produced a significant change in pulse rate 20 minutes after administration as compared to diazepam.
2. A significant difference of the effect of blood pressure (both systolic and diastolic) was noted between diazepam and nifedipine-diazepam combination as early as 20 minutes after administration.
3. The mean arterial pressure however, remained fairly stationary and statistically insignificant($p > 0.05$).

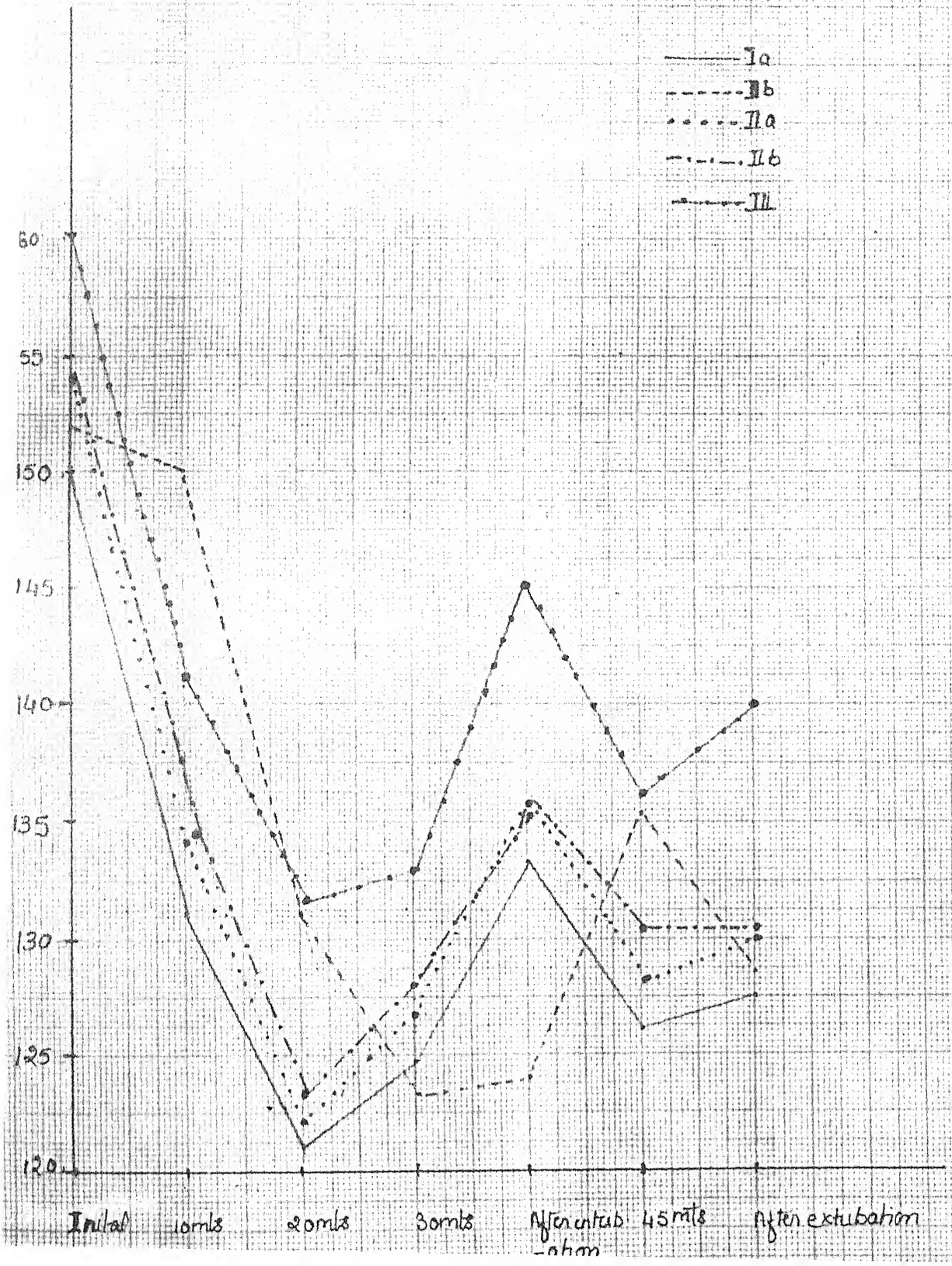
On comparing group IIa and III the effect of nifedipine with nifedipine-diazepam combination during general anaesthesia in group IIa and III (Table XI), it was seen that :-

1. Nifedipine and nifedipine-diazepam combination produced a significant change in pulse rate 10 minutes after administration and highly significant at 30 minutes.
2. A significant difference of the effect on blood pressure (both systolic and diastolic) was noted between nifedipine and nifedipine-diazepam combination as 20 minutes after administration.
3. Mean arterial pressure however, remained fairly stationary and statistically insignificant($p > 0.05$).

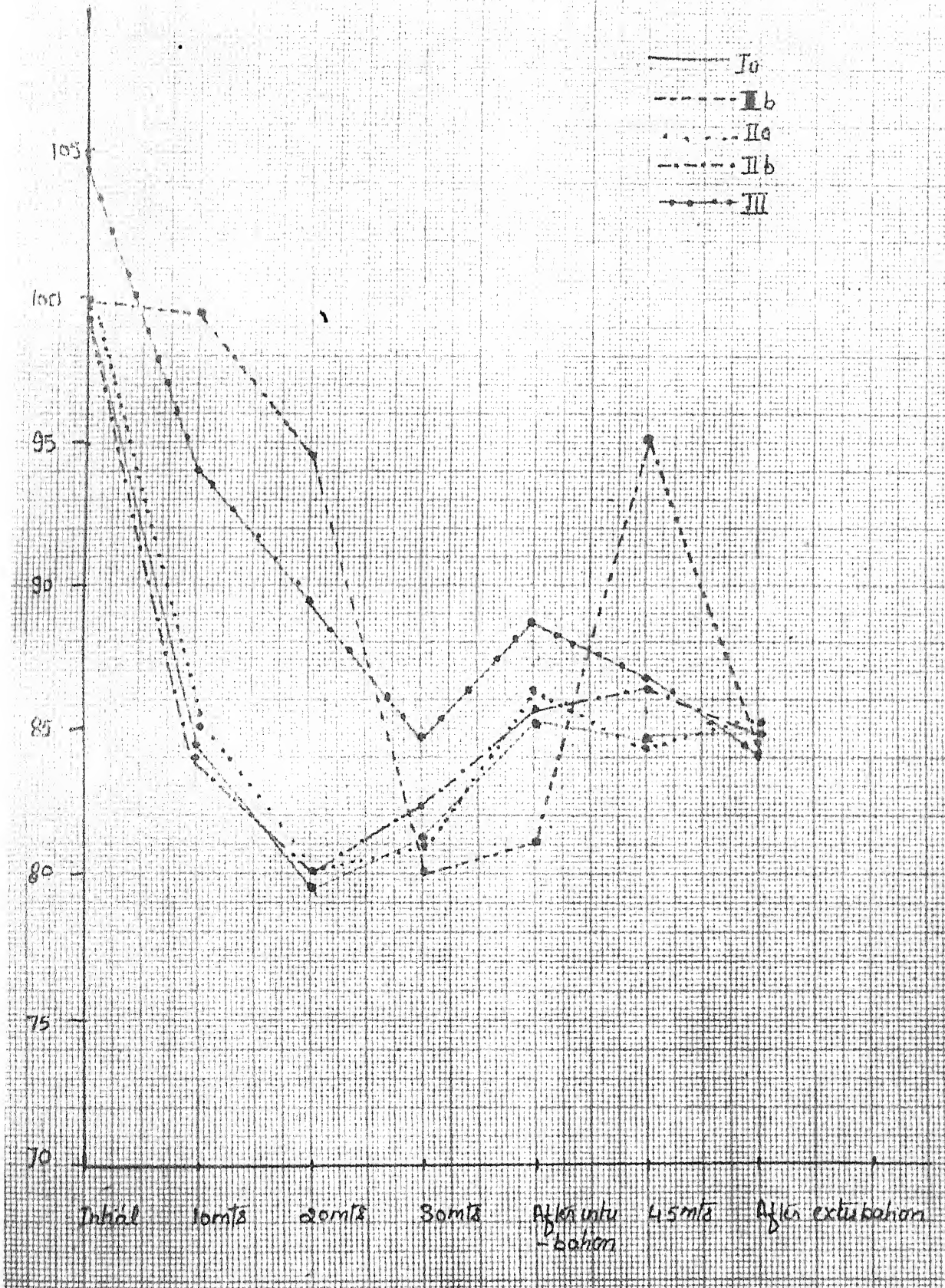
GRAPH SHOWING CHANGES IN PULSE RATE IN VARIOUS GROUPS



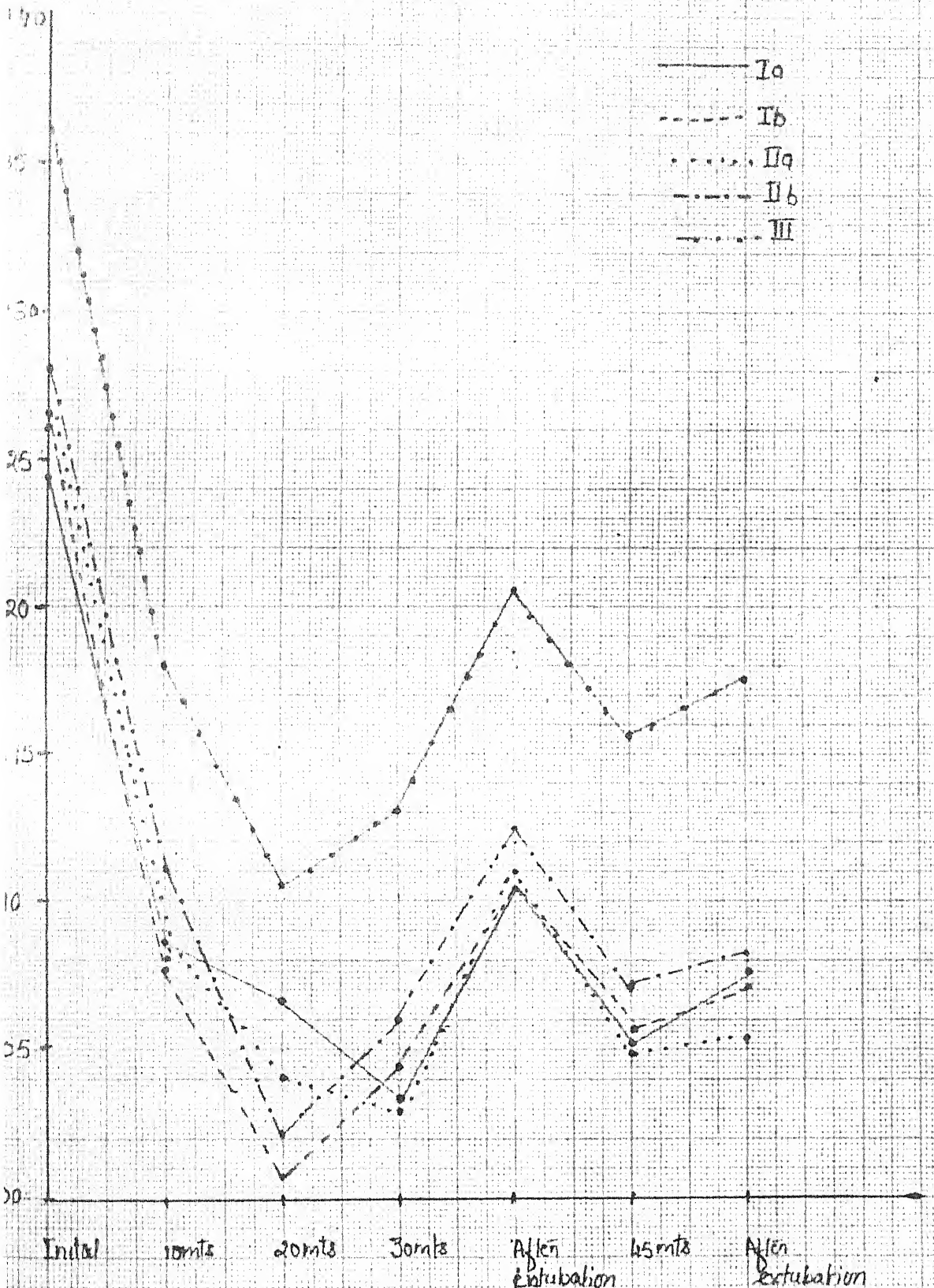
GRAPH SHOWING CHANGES IN SYSTOLIC BLOOD PRESSURE IN VARIOUS GROUPS



GRAPH SHOWING CHANGES IN DIASTOLIC BLOOD PRESSURE IN VARIOUS GROUPS



GRAPH SHOWING CHANGES IN MEAN ARTERIAL PRESSURE IN VARIOUS GROUPS



D I S C U S S I O N

D I S C U S S I O N

High blood pressure in association with pregnancy has long been regarded as an omnious sign. Kaplan et al (1962) reviewed chronic renal diseases and hypertension associated with pregnancy and advised that therapeutic abortion should be carried out, if the blood pressure rises to 160/100mm Hg. Fiarly and Kincaid Smith (1968) concluded that morbidity and mortality rates(mainly relating to the foetus) were increased in the presence of hypertension.

Prevention and treatment of pregnancy induced hypertension have learned in the last 10 years. High blood pressure complicated approximately 10% of all pregnancies. Pre-eclampsia, the association of hypertension proteinuria and oedema, accounts for more than 50% of all the hypertensive disorders of pregnancy and is a major cause of foetal and maternal morbidity and mortality.

Hypertension in pregnancy treated as :-

1. Na restriction, bed rest.
2. Elucidation of some of the mechanisms responsible for blood pressure elevation in pregnancy has permitted therapy to be based on more rational principles.
3. Anti hypertensive therapy using sympathetic inhibition with either methyldopa or alpha and beta adrenoceptor blockage.

Vasodilation with hydralazine, calcium entry, blockers (nifedipine) intravenous labetalol or diazoxide is primarily used in severely hypertensive patients.

4. During long term antihypertensive therapy, treatment with pindolol yielded better foetal growth than therapy with atenolol.

Aim of this study was to evaluate the effect of nifedipine in pregnancy induced hypertension. Patients with pregnancy induced hypertension who were scheduled for emergency caesarean section procedures requiring general anaesthesia and spinal anaesthesia were selected for the study. Very few studies have been reported in which such drug and combination of drugs have been used for this purpose.

Numerous techniques and agents have been employed for this purpose but none was found to be 100% successful.

Beta blockers were also studied very extensively. Pry's Roberts et al (1969) reported that propanolol was effective in suppressing the cardiovascular response to tracheal and nasopharyngeal suction of secretion in tetanus patients.

Protocol (Prys-Roberts, 1973) given intravenous or orally was shown to be effective in suppressing the pressor responses to laryngoscopy and intubation. Metoprolol, a cardioselective beta blocker was

shown to be reducing arterial pressure during intubation and after extubation (Magnusson et al, 1986).

Sodium nitroprusside (Stoelting, 1979) intranasal nitroglycerine (Fassoulabi and Kanaris, 1973; Kolak et al, 1986), Isosorbide dinitrate (Hatano et al, 1989), trimetaphan (Saitoh et al, 1991) were all found to be reducing the magnitude of the rise in blood pressure but the associated tachycardia was not prevented.

Smith et al (1982) employed hydrallazine and diazoxide in severe hypertension, but there were certain limitations associated with the use of these agents as they have to be administered parenterally and there is high incidence of side effects of the use of these agents at times it become extremely difficult to control hypertension in pregnancy with conventional antihypertensive drugs. Antihypertensive therapy utilizing sympathetic inhibition with either methyldopa or alpha and beta adrenoceptor blockade yield, and the most promising results vasodilation with hydralazine calcium entry blockers (nifedipine) intravenous labetalol or diazoxide is primarily used in severely hypertensive patients. The use of orally administered nifedipine in severely hypertensive women is associated with encouraging results.

It is clear that women with blood pressure levels greater than 170/110 mm Hg need antihypertensive therapy for maternal safety. It remains to be proven to

what extent foetal growth and welfare can be improved in women with diastolic pressure levels 85-110 mm Hg when adrenoceptor blocking agents and used for blood pressure control. Initial studies were suggestive of improved foetal growth, prevention of proteinemia and the respiratory distress syndrome but more long term controlled studies are required.

Chronic hypertension is treated with methyldopa and PIH is treated with atenolol. There is evidence that therapy is beneficial in terms of immediate pregnancy outcome and is not harmful to the child. Atenolol is currently being evaluated in combination with nifedipine to treat cases of early onset of severe pre-eclampsia and preliminary results and are encouraging prevention rather than cure should be the aim in managing hypertensive diseases during pregnancy. Early intervention can prevent serious problem later on (Rubin, 1990).

Of the calcium channel blocking agent nifedipine was found to be very effective in reducing the pressor response (Khan et al, 1987; 1989; Puri and Batra, 1988; Bhola and Abraham, 1990). Varapanil was not as effective as nifedipine and also a significant prolongation of P-R interval was observed in some patients (Kolli et al,1987; Rashid Khan et al, 1989). Diltiozem was reported to be unsuccessful in this respect (Chandralekha et al, 1990).

In the present study sublingual nifedipine was used alone and in combination with diazepam each to

decrease the pulse rate and systolic & diastolic blood pressure. Use of any of the drugs or drug combination decrease significant reduction in systolic blood pressure and diastolic blood pressure, pulse rate following laryngoscopy and tracheal intubation.

Huysmans et al (1983) emphasized an advantage of a calcium antagonist in comparison to other vasodilators that it selectively increases cerebral and cardiac blood flow, as nas been shown in human. Data of present study further suggest that a short term use of nifedipine does not appear to compromise neonatal outcome. Therefore, nifedipine appears to be safe and effective antihypertensive agent for short term use in acute obstetric hypertension because of ease of administration, rapid onset and long duration of action.

The results of this study showed that the blood pressure was significantly lowered after diazepam intramuscularly after sublingual administration of nifedipine in patients with pregnancy induced hypertension presenting for surgery. The peak effect occurred in 30 minutes. The effect was sustained and the blood pressure remained stable throughout the period of anaesthesia. The blood pressure did not rise on. In fact, it remained well below the value with patient had presented. There was no significant change in pulse rate also. But Zusman et al (1987) reported a rise of 3.7 to 6.7% in pulse rate in

nifedipine treated patients during anaesthesia and operation. The finding of this study confirmed the observations reported by Zusman et al (1987) and Jain et al (1987).

Since nifedipine has also a coronary vasodilating action it may be useful in patients with coronary spasm (Reis et al, 1982). Thus nifedipine acquired a special usefulness in the perioperative period in hypertensive patients.

All patients who received nifedipine showed significant reduction in both systolic blood pressure and diastolic blood pressure. In patients who received diazepam showed adequate fall in blood pressure.

It is evident from this study that in all pregnant women having severe hypertension the response to diazepam and nifedipine was adequate. When nifedipine was administered to these patients a significant reduction in both systolic and diastolic blood pressure was observed. These results concus with the findings of earlier workers (Rubin et al, 1984) who in their uncontrolled study have shown the effectiveness of nifedipine in severe hypertension in pregnancy unresponsive to beta blockers. In the present study, nifedipine seemed to be better antihypertensive agent as all the patients who received nifedipine as initial therapy responded to it and patients who responded to diazepam no acute adverse effects on foetal outcome were observed with nifedipine.

Dulilzhy et al (1986) and Martenells et al(1986) showed that nifedipine when used alone was effective and safe in pregnancy. Constantine et al (1987) used slow release nifedipine with atenolol and alpha-methyldopa in 23 hypertensive females and found this combination useful.

A maximum fall in blood pressure was observed between 30 minutes and 3 hours after administration of nifedipine which was at variance to the results of other workers (Walkers and Redman, 1984) who observed the maximum fall between 20 to 30 minutes. With present knowledge it appeared very difficult to explain this variability in present.

At present no other anti-hypertensive drug is available in India which can be effective in lowering the blood pressure in hypertensive emergencies during pregnancy within 30 minutes. Nifedipine can lower the blood pressure within 20 to 30 minutes and has no adverse effect on foetus (Jain et al, 1987). Therefore, this drug can be useful addition to the armamentarium of antihypertensive drugs used in pregnancy.

Nifedipine exerts little or no effect on the blood pressure in normotensive subject (Stone et al, 1980). However, it is highly effective in the acute treatment of moderate to severe elevation of blood pressure where it produces a reliable reduction in systolic and diastolic pressures (Beer et al, 1981).

When nifedipine was administered orally or sublingually 90% of the drug is absorbed. The drug is detectable in the serum 3 minutes after the sublingual and 20 minutes after the oral administration effect in 30-60 minutes which lasts for 6-10 hours (Aobi et al, 1978; Kawajima et al, 1978). When given sublingually 10 mg nifedipine lowers blood pressure marking 15 minutes after its administration and the effect lasts for 90 minutes (Stone et al, 1980).

Schewitiz (1971) observed hypertensive pregnant patients and showed contradictory results with sodium and water homeostasis. The use of diuretics may well have distorted some of the results where no increase or even depletion of sodium and water was reported. The accepted view at present is that hypertensive mothers have smaller increase in plasma volume, total exchangeable sodium and extracellular fluid than normal pregnant women (Chesley, 1972). These observations made it difficult to believe that sodium and water retention can be an important primary factor in the causation of pregnancy related hypertension.

Nifedipine reduces both systolic and diastolic blood pressure with a minimal amount of side effects including orthostasis (Spurrell et al, 1974). Nifedipine also induces a powerful basoreceptor mediated reflex beta-adrenergic response to affect its negative ionotropic action and thus enhancing ventricular performance

(Ellrodt et al, 1980). It suggests a state of tachycardia in the patients treated with nifedipine but in the present study the average pre-operative pulse rate was only 86.5± 6.1. This did not cause any concern and the response at intubation was only a subdued like. Reported side effects of nifedipine are hypotension tachycardia and A.V. conduction blockage, none of which was present pre-operatively in the patients in this study.

Stone et al (1980) have evaluated the efficacy of a single oral or sublingual dose of nifedipine in preventing the rise in pulse and blood pressure induced by laryngoscopy and endotracheal intubation. Nifedipine exerts little or no effect on the blood pressure in normotensive subjects. When given sublingually 10 mg nifedipine lowers blood pressure markedly, 15 minutes after its administration and the effect lasts for 90 minutes.

Kawajuna et al (1978), Aobi et al, (1978) observed when nifedipine is administered orally or sublingually 90% of the drug is absorbed. The drug is detectable in the serum 3 minutes after the sublingual and 20 minutes after the oral administration on oral nifedipine (10 mg) exerts the peak haemodynamic effects in 30-60 minutes which lasts for 6-10 hours.

Smith et al (1982) in severe hypertension, hydrallazine and diazoxide are employed but there are certain limitations associated with the use of these

agents as they have to be administered parenterally and there is high incidence of side effects the use of these agents at times it becomes extremely difficult to control hypertension in pregnancy with conventional antihypertensive drugs.

Reves et al (1982) oral nifedipine attenuated the pressure response only to a limited extent. It is likely that gastric absorption of nifedipine in the perioperative period was erratic and effective blood levels were not achieved. Sublingual nifedipine proved to be significantly more effective in checking the rise in mean arterial pressure. But nifedipine did not check the rise in pulse rate. This was probably because nifedipine is devoid of any effect on the A.V. nodal conduction. But despite this drawback in nifedipine, the rate pressure product, which is an index of myocardial O_2 demand remains lower in nifedipine treated subjects.

Nifedipine is a calcium channel blocker. Its clinical use since 1973 had been found to be effective and safe in patients having moderate to severe essential hypertension (Murphy et al, 1983).

Nifedipine acts by blocking calcium entry to the smooth muscles. Thus interefere with excitation and contraction coupling given orally it was rapid onset of action and low incidence of serious side effects.

Nifedipine has been used in pregnancy for inhibition uterine contractions in preterm labour and prosta-

glandins induced termination of pregnancy where there was uterine hypotonus (Anderson et al, 1979). Its onset of action was not longer than 20 minutes. Hypotensive effect lasted at least 4 hours after 10 mg of nifedipine by mouth. No significant potentiation of the action of nifedipine with administration of other hypotensive agent was seen.

Nifedipine when combined with propanolol is highly effective because observed increase in heart rate with nifedipine is inhibited by propanolol probably by inhibiting the cardicvascular effects of the activity of the sympathetic nervous system.

Blood pressure is significantly after sublingual administration of nifedipine in patients with controlled hypertension. The effect is sustained and the blood pressure remains stable throughout the period of anaesthesia. The blood pressure does not rise to alarming level and even at the time of intubation or extubation. There is not significant change in pulse rate also. But Zusman et al (1987) reported a rise of 3.7 to 6.7% in pulse rate in nifedipine treated patients during anaesthesia and operation. The finding of present study confirm the observations reported by Zusman et al (1987) and Jain et al (1987).

Ahokas et al (1988) studied nifedipine (200 microgram/kg) effectively lowered mean arterial pressure 25% by decreasing total peripheral resistance 38% cardiac output was increased 15% blood flows to the splanchnic

region and the reproductive organs were increased after nifedipine administration. The increase in blood flow to the reproductive organs was the result of increased ovarian and uterine wall perfusion blood flow was not significantly altered, but resistance was decreased. Thus the use of nifedipine to lower maternal blood pressure in pregnancy complicated by extreme hypertension does not necessarily decrease uteroplacental blood flow.

The effect of nifedipine (Adalat Bayes Miles) a calcium channel blockers, which has a well established place in nonobstetric hypertension was compared with dihydralazine in 33 primigravidas with severe hypertension of pregnancy. Patients with a diastolic blood pressure greater than 110 mm Hg before or during administration were randomly assigned to treatment with either nifedipine or dihydralazine. Both drugs were found to be equally efficacious. Nifedipine, however, showed an earlier onset of action in lowering systolic blood pressure and had the advantage of oral administrations.

Nifedipine is an antagonist of calcium influx through slow channel of the cell membrane. Its hypotensive action is mainly due to dilatation of the arterial resistance vessels. Dose and route of administration of the drug used in this study were same as that used by Puri and Batra (1988) and Khan et al (1987). Nifedipine prevented the rise in mean arterial pressure significantly.

The rise in mean arterial pressure from the basal to the maximum recorded value in the control group was 43.3% of the basal and in the nifedipine group 21.74% compared with buprenorphine nifedipine produced a significantly higher reduction in maximum rise in mean arterial pressure ($p < 0.05$). Three minutes after intubation the mean arterial pressure was significantly lower than that of control, lignocaine or buprenorphine groups ($p < 0.05$). The increase in rate pressure product in the nifedipine group was also lesser than in the buprenorphine one, but the difference was insignificant.

In the present study, nifedipine effectively lowered the blood pressure. Its onset of action was prompt, not longer than 20 minutes in most instances, but the spontaneous subsidence of spiker of high blood pressure is often observed. For this reason the entry criteria specified that the hypertension should be sustained over at least 20 minutes. The hypotensive effect lasted at least 4 hour after 10 mg of nifedipine by mouth. No significant potentiation of the action of nifedipine with concurrent administration of other hypotensive agents was seen contrary to the effects described in non pregnant patients (Gudzzi et al, 1980).

No serious side effects were observed with nifedipine, mild to moderate headache and palpitation could not be specifically correlated with use of

nifedipine alone as former should be a manifestation of severe PIH / or eclampsia and later could result from magnesium sulfate therapy as well. Most of the other side effects like insignificant rise in pulse rate and occurrence of flushing are expected consequence of the vasodilatation effect of nifedipine by which it exerts antihypertensive action (Huysmans et al, 1983).

The three drug combination used were lignocaine+ buprenorphine, lignocaine + nifedipine and buprenorphine+ nifedipine. A combined effect of each of the individual drugs were expected with this technique. But in fact the study failed to demonstrate any such additive effects. There was no significant difference in the mean heart rate values. The degree of reduction in maximum rise in mean arterial pressure with the drug combination stool close to the effect of that particular individual drug of the combination which showed a better effect than the other when used alone.

All 90 patients who received either diazepam or nifedipine or diazepam nifedipine combination showed significant reduction in both systolic and diastolic blood pressure. There was a significant decrease in pulse rate in all groups after atropine, diazepam nifedipine premedication.

Mean basal pulse rate of any group were not significantly different. Following laryngoscopy and intubation pulse rate decreased very significantly in

all groups reaching a maximum reduction at 30 minutes after premedicant and decreased gradually over the next 15 minutes. Pulse rate decreased after diazepam premedication intramuscularly in general anaesthesia was 93±7 minutes but in spinal analgesia the pulse rate was 95±4 minutes.

The maximum decrease in pulse rate who received nifedipine sublingually with general anaesthesia and spinal anaesthesia was 88±9/minute and 94±8/minute respectively.

The maximum decrease in pulse rate who received diazepam and nifedipine combination in general anaesthesia was 98±8/min.

Mean systolic blood pressure maximally decrease after diazepam in general anaesthesia and spinal analgesia was 121.68±4.095 mm Hg just after intubation, 120.4±4.2 after 45 minutes.

Maximum decrease in mean systolic blood pressure after nifedipine in general and spinal anaesthesia was 122.68±4.8 after 20 minutes and 123.4±4.8 after 20 minutes.

Maximum decrease in mean systolic blood pressure after diazepam + nifedipine combination in general anaesthesia was 110.4±33.4 mmHg.

Maximum decrease in mean diastolic blood pressure after diazepam in general and spinal anaesthesua was 79.6±2.15 after 20 minutes and 79.8±2.14 after 30 minutes.

Maximum decrease in mean diastolic blood pressure after nifedipine in general and spinal anaesthesia was 80.1±2.2 and 80.4±2.2 respectively after 20 minutes.

Maximum decrease in mean diastolic blood pressure after diazepam + nifedipine combination in general anaesthesia was 84.82±4.1 after 30 minutes of diazepam+nifedipine. There was no significant decrease in mean arterial blood pressure ($p > 0.05$) in all groups.

No complication like hypotension or bradycardia were noted in any of the patients during the subsequent period of anaesthesia. This is especially important with the view that volatile anaesthetic agents can potentiate the effect of calcium channel blockers.

This study shows that both diazepam and nifedipine are effective in decreasing the pulse rate in group Ia and IIa, systolic blood pressure and diastolic blood pressure and nifedipine provides a statistically better response than diazepam.

When diazepam was used in combination of nifedipine no added advantage or a better effect could be demonstrated. A safe agent or technique that can prevent the increase in pulse rate, systolic blood pressure, diastolic blood pressure is yet to be found out and more researches have to be carried out in this regard.

C O N C L U S I O N

CONCLUSION

This study was conducted in 90 pregnancy induced hypertensive patients for emergency caesarean section requiring general anaesthesia or spinal analgesia.

In conclusion, data of present study suggest that nifedipine as premedicant adequately controls pregnancy induced hypertension in emergency caesarean section during anaesthesia.

In this study, efficacy of a single dose of 10 mg nifedipine administered pre-operatively by sublingual routes was evaluated to attenuate the hypertensive and tachycardia response to laryngoscopy and endotracheal intubation. Sublingual nifedipine proved to be significantly more effective in checking the rise in mean arterial pressure.

Aim of the study was to determine the effect of diazepam and nifedipine and combination of nifedipine and diazepam as premedicant in pregnancy induced hypertension. From the analysis of the observation in the present study the following conclusions were drawn.

- When pregnancy induced hypertensive patients anaesthetised with thiopentone and suxamethonium laryngoscopy and tracheal intubation evokes a cardiovascular response in the form of tachycardia and hypertension which is maximum at 1 minute after intubation.
- Diazepam 10 mg administered intramuscularly half an hour after induction was more effective in preventing

the rise in mean arterial pressure. The rise in pulse rate also prevented by administration of diazepam. Three to eight beats per minute was lowered by diazepam.

- Nifedipine 10 mg administered sublingually half an hour before induction was more effective in preventing the rise in mean arterial pressure 36-37 mm Hg, the rise in pulse rate was also prevented by administration of nifedipine. But more decrease in mean arterial pressure and pulse rate with nifedipine was observed.
- When these drugs were used in combination no added effect could be demonstrated. The effect of nifedipine and diazepam combination was almost similar to that of nifedipine alone.

In other words the degree of reduction in maximum fall in mean arterial pressure with the nifedipine which showed a better effect than the diazepam.

- Of all the drugs and drug combination used in this study nifedipine was most effective as premedicant in pregnancy induced hypertension. A significant difference of the effect on blood pressure (both systolic and diastolic) was noted between diazepam and nifedipine as early as 10 minutes after administration. Thus, diazepam showed a potent hypotensive effect in a short time as with nifedipine.

The mean arterial pressure however remained fairly stationary after administration of diazepam, nifedipine and diazepam+nifedipine combination ($p > 0.05$).

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